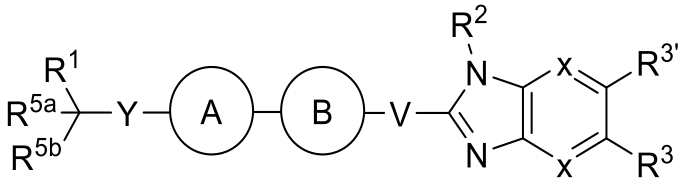
WHAT IS CLAIMED IS:

1. A compound of Formula I-A-1:



(I-A-1)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -S-R^{1b}, -S(O)R^{1b}, -S(O)(NH)R^{1b}, -$S(O)_2R^{1b}$, -$S(O)_2N(R^{1b})(R^{1c})$, -S(O)$(NR^{1b})R^{1c}$, -C(O)$N(R^{1b})(R^{1c})$, -C(O)R^{1b}, or -C(O)OR^{1c}, wherein the alkyl, haloalkyl, cycloalkyl, aryl, 5-10 membered heteroaryl, or heterocyclyl is each optionally substituted with one to four Z^1, and wherein any two Z^1 can be combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl or C_{6-10} aryl or 5-10 membered heteroaryl;

Ring A is C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl or 5-10 membered heteroaryl, which is each optionally substituted with one to four Z^{1a};

Ring B is C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl or 5-10 membered heteroaryl, which is each optionally substituted with one to four R^4;

Ring A and Ring B each contains zero to three double bonds;

R^2 is H, C_{1-6} alkyl, -C_{1-6} alkyl-alkoxy, -C_{1-6} alkyl-cycloalkoxy, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -OR^{2a}, -S-R^{2a}, -S(O)R^{2a}, -S(O)$(NH)R^{2a}$, -$S(O)_2R^{2a}$, -$S(O)_2N(R^{2a})(R^{2b})$, or -S(O)$(NR^{2a})R^{2b}$, wherein the alkyl, alkoxy, cycloalkoxy, haloalkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^1, and wherein any two Z_1 can be combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl or C_{6-10} aryl or 5-10 membered heteroaryl;

X is each independently -N=, -C(H)=, or -C(R^8)=;

each R^3 and $R^{3'}$is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -NO_2, -OR^{3a}, -C(O)R^{3a}, -CH_2C(O)OR^{3a}, -C(O)OR^{3a}, -C(O)N(R^{3a})(R^{3b}), -N(R^{3a})C(O)R^{3b}, -N(R^{3a})C(O)OR^{3b}, -N(R^{3a})C(O)N$(R^{3b})_2$, -C(O)NHS$(O)_2R^{3a}$, - C(O)NR^{3a}S$(O)_2R^{3b}$, -C(O)NR^{3a}S$(O)_2$N$R^{3b}R^{3c}$, -C(O)NR^{3a}-S(O)(=NR^{3b})R^{3c}, -$S(O)_2R^{3a}$, -$S(O)_2OR^{3a}$, -

$S(O)_2N(R^{3a})(R^{3b})$, $-N(R^{3a})S(O)_2R^{3b}$, $-S(O)_2NHC(O)R^{3a}$, $-S(O)(=NR^{3a})R^{3b}$, $-S(O)(=NR^{3a})NR^{3b}$, $-S(=NR^{3a})(=NR^{3b})R^{3c}$, $-P(O)(OR^{3a})(R^{3b})$, $-P(O)(OR^{3a})(OR^{3b})$, $-B(OR^{3a})(OR^{3b})$, or $-O-C_{1-6}$alkyl-$C(O)OR^{3a}$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four R^{3d};

each R^{3a}, R^{3b}, and R^{3c} is independently H, C_{1-6} alkyl, C_{6-10} aryl, 5-10 membered heteroaryl, C_{1-6} haloalkyl, C_{2-8} alkoxyalkyl, $-C_{1-4}$ alkyl-$N(R^{9a})(R^{9b})$, $-C_{1-4}$ alkyl-$N(R^{9a})C(O)-O-C_{1-4}$ alkyl-$OP(O)(OR^{9c})_2$, $-C_{1-4}$ alkyl-$C(O)N(R^{9a})(R^{9b})$, $-C_{1-4}$ alkyl-$O-C(O)-O-C_{1-4}$ alkyl, $-C_{1-4}$ alkyl-$O-C(O)-C_{1-4}$ alkyl-$N(R^{9a})(R^{9b})$, $-C_{1-4}$ alkyl-$O-C(O)-C_{1-4}$ alkyl- $OP(O)(OR^{9c})_2$, $-C_{1-4}$ alkyl-C_{3-8} cycloalkyl, $-C_{1-4}$ alkyl-heterocyclyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, $-CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, $-P(O)(OR^{9c})_2$, $-OP(O)(OR^{9c})_2$, $-CH_2P(O)(OR^{9c})_2$, $-CH_2OP(O)(OR^{9c})_2$, $-OCH_2P(O)(OR^{9c})_2$, $-C(O)OCH_2P(O)(OR^{9c})_2$, $-P(O)(R^{9c})(OR^{9d})$, $-OP(O)(R^{9c})(OR^{9d})$, $-CH_2P(O)(R^{9c})(OR^{9d})$, $-OCH_2P(O)(R^{9c})(OR^{9d})$, $-C(O)OCH_2P(O)(R^{9c})(OR^{9d})$, $-P(O)(N(R^{9c})_2)_2$, $-OP(O)(N(R^{9c})_2)_2$, $-CH_2P(O)(N(R^{9c})_2)_2$, $-OCH_2P(O)(N(R^{9c})_2)_2$, $-C(O)OCH_2P(O)(N(R^{9c})_2)_2$, $-P(O)(N(R^{9c})_2)(OR^{9d})$, $-OP(O)(N(R^{9c})_2)(OR^{9d})$, $-CH_2P(O)(N(R^{9c})_2)(OR^{9d})$, $-OCH_2P(O)(N(R^{9c})_2)(OR^{9d})$, $-C(O)OCH_2P(O)(N(R^{9c})_2)(OR^{9d})$, $-P(O)(R^{9c})(N(R^{9d})_2)$, $-OP(O)(R^{9c})(N(R^{9d})_2)$, $-CH_2P(O)(R^{9c})(N(R^{9d})_2)$, $-OCH_2P(O)(R^{9c})(N(R^{9d})_2)$, $-C(O)OCH_2P(O)(R^{9c})(N(R^{9d})_2)$, C_{1-6} alkyl-heterocyclyl, C_{1-6} alkyl-aryl, or C_{1-6} alkyl-(5-10 membered) heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each R^4 is independently H, -OH, CH_2OH, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, $-O-R^{4a}$, $-C(O)R^{4a}$, $-C(O)O-R^{4a}$, $-C(O)N(R^{4a})(R^{4b})$, $-N(R^{4a})(R^{4b})$, $-N(R^{4a})_2(R^{4b})^+$, $-N(R^{4a})-C(O)R^{4b}$, $-N(R^{4a})C(O)O(R^{4b})$, $-N(R^{4a})C(O)N(R^{4b})(R^{4c})$, $-N(R^{4a})S(O)_2(R^{4b})$, $-N(R^{4a})S(O)_2-N(R^{4b})(R^{4c})$, $-N(R^{4a})S(O)_2O(R^{4b})$, $-OC(O)R^{4a}$, $-OC(O)OR^{4a}$, $-OC(O)-N(R^{4a})(R^{4b})$, $-S-R^{4a}$, $-S(O)R^{4a}$, $-S(O)(NH)R^{4a}$, $-S(O)_2R^{4a}$, $-S(O)_2N(R^{4a})(R^{4b})$, $-S(O)(NR^{4a})R^{4b}$, or $-Si(R^{4a})_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; or two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four Z^{1b};

each R^{5a} and R^{5b} is independently H, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, $-C_{1-6}$ alkyl-$N(R^{9a})(R^{9b})$, -CN, $-OR^{5a1}$, or

-N(R^{5a1})(R^{5a2}); or R^{5a} and R^{5b} are combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{5a3}; or R^{5a} or R^{5b} can be combined with the substituents on Ring A to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{5a3};

each R^{5a1} and R^{5a2} is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four R^{5a4};

V is -C(O)-, -O-, -N(R^{6a})-, or -C(R^{6b})(R^{6c})-;

R^{6a} is H, C_{1-6} alkyl, C_{3-10} cycloalkyl, heterocyclyl, -S(O)$_2$$R^{6a1}$, or -S(O)$_2$N($R^{6a1}$)($R^{6a2}$), wherein the cycloalkyl or heterocyclyl in each instance is optionally substituted with C_{1-6} alkyl, F, or -CN;

each R^{6b} and R^{6c} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, -C_{1-6} alkyl-N(R^{9a})(R^{9b}), -CN, -OR^{6c1}, or -N(R^{6c2})(R^{6c3}), wherein the alkyl, cycloalkyl, or heterocyclyl in each instance is optionally substituted with one to four R^{6b1}; or R^{6b} and R^{6c} are combined with the atom to which they are attached to form C_{3-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{6b1}; or R^{6a} or R^{6c} is combined with one R^4 group and the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{10};

Y is -N(R^7)-, -O-, -S-, -S(O)-, -S(O)$_2$-, -S(O)(=NH)-, or -S(O)(=NR^7)-;

each R^{3d}, R^{5a3}, R^{5a4}, R^{6b1}, and R^{10} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, or -C(O)N(R^{2a})(R^{2b}), wherein the heterocyclyl or 5-10 membered heteroaryl in each instance is optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

each R^{6a1}, R^{6a2}, R^{6c1}, R^{6c2}, R^{6c3} and R^7 is independently H, C_{1-6} alkyl or C_{3-10} cycloalkyl;

each R^8 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$;

each R^{9a} and R^{9b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a},

-C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$;

or R^{9a} and R^{9b} together form a 3-10 membered heterocyclyl optionally substituted with C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$;

each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -N_3, -CN, -O-R^{12a}, -C(O)-R^{12a}, -C(O)O-R^{12a}, -C(O)-N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})C(O)-R^{12b}, -N(R^{12a})C(O)O-R^{12b}, -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -NR^{12a}S(O)$_2$N(R^{12b})(R^{12c}), -NR^{12a}S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1a};

each Z^{1a} is independently H, -OH, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each Z^{1b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{2-6} alkenyl), -O(C_{2-6}

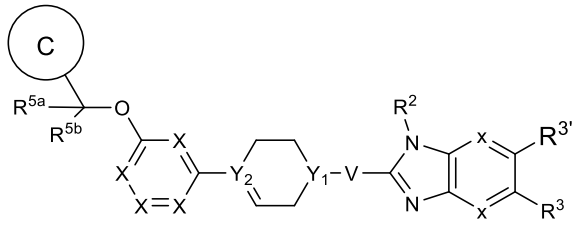
alkynyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(C_{6-10} aryl), -O(5-10 membered heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{2-6} alkenyl), -NH(C_{2-6} alkynyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(C_{6-10} aryl), -NH(5-10 membered heteroaryl), -N(cyclo-alkyl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$, -N(C_{2-6} alkenyl)$_2$, -N(C_{2-6} alkynyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -N(heterocyclyl)$_2$, -N(C_{6-10} aryl)$_2$, -N(5-10 membered heteroaryl)$_2$, -N(C_{1-9} alkyl)(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)(C_{2-6} alkenyl), -N(C_{1-9} alkyl)(C_{2-6} alkynyl), -N(C_{1-9} alkyl)(C_{3-15} cycloalkyl), -N(C_{1-9} alkyl)(heterocyclyl), -N(C_{1-9} alkyl)(C_{6-10} aryl), -N(C_{1-9} alkyl)(5-10 membered heteroaryl), -C(O)(C_{1-9} alkyl), -C(O)(C_{1-8} haloalkyl), -C(O)(C_{2-6} alkenyl), -C(O)(C_{2-6} alkynyl), -C(O)(C_{3-15} cycloalkyl), -C(O)(heterocyclyl), -C(O)(C_{6-10} aryl), -C(O)(5-10 membered heteroaryl), -C(O)O(C_{1-9} alkyl), -C(O)O(C_{1-8} haloalkyl), -C(O)O(C_{2-6} alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(5-10 membered heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(5-10 membered heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(5-10 membered heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl),-NHC(O)O(C_{6-10} aryl), -NHC(O)O(5-10 membered heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), -NHC(O)NH(5-10 membered heteroaryl), -NHS(O)(C_{1-9} alkyl), -N(C_{1-9} alkyl)(S(O)(C_{1-9} alkyl), -S(C_{1-9} alkyl), -S(C_{1-8} haloalkyl), -S(C_{2-6} alkenyl), -S(C_{2-6} alkynyl), -S(C_{3-15} cycloalkyl), -S(heterocyclyl), -S(C_{6-10} aryl), -S(5-10 membered heteroaryl), -S(O)N(C_{1-9} alkyl)$_2$, -S(O)(C_{1-9} alkyl), -S(O)(C_{1-8} haloalkyl), -S(O)(C_{2-6} alkenyl), -S(O)(C_{2-6} alkynyl), -S(O)(C_{3-15} cycloalkyl), -S(O)(heterocyclyl), -S(O)(C_{6-10} aryl), -S(O)(5-10 membered heteroaryl), -S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{2-6} alkenyl), -S(O)$_2$(C_{2-6} alkynyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(C_{6-10} aryl), -S(O)$_2$(5-10 membered heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$, wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H,-O(C_{1-9} alkyl), -O(C_{1-8}

haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(5-10 membered heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(5-10 membered heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(5-10 membered heteroaryl), -NHC(O)NH(C_{1-9} alkyl), S(O)$_2$(C_{1-9} alkyl), -S(O)$_2$(C_{1-8} haloalkyl), -S(O)$_2$(C_{3-15} cycloalkyl), -S(O)$_2$(heterocyclyl), -S(O)$_2$(aryl), -S(O)$_2$(5-10 membered heteroaryl), -S(O)(NH)(C_{1-9} alkyl), -S(O)$_2$NH(C_{1-9} alkyl), or -S(O)$_2$N(C_{1-9} alkyl)$_2$;

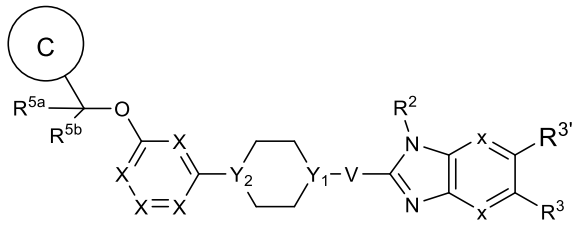
each R^{1b}, R^{1c}, R^{2a}, R^{2b}, R^{4a}, R^{4b}, R^{4c}, R^{9c}, R^{9d}, R^{12a}, R^{12b}, and R^{12c} is independently H, -OH, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; and

each R^{3e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, -C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C(O)N(R^{9a})(R^{9b}), -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -P(O)(OR^{9c})$_2$, -CH_2P(O)(OR^{9c})$_2$, -OCH_2P(O)(OR^{9c})$_2$, -C(O)OCH_2P(O)(OR^{9c})$_2$, -P(O)(R^{9c})(OR^{9d}), -OP(O)(R^{9c})(OR^{9d}), -CH_2P(O)(R^{9c})(OR^{9d}), -C(O)OCH_2P(O)(R^{9c})(OR^{9d}), -P(O)(N(R^{9c})$_2$)$_2$, -CH_2P(O)(N(R^{9c})$_2$)$_2$, -C(O)OCH_2P(O)(N(R^{9c})$_2$)$_2$, -P(O)(N(R^{9c})$_2$)(OR^{9d}), -CH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -C(O)OCH_2P(O)(N(R^{9c})$_2$)(OR^{9d}), -P(O)(R^{9c})(N(R^{9d})$_2$), -CH_2P(O)(R^{9c})(N(R^{9d})$_2$), or -C(O)OCH_2P(O)(R^{9c})(N(R^{9d})$_2$), wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; wherein each 5-10 membered heteroaryl has 5 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S; and wherein each heterocyclyl has 3 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is a compound of Formula I-A-2 or Formula I-A-3



(I-A-2)



(I-A-3)

, wherein

Ring C is C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl or 5-10 membered heteroaryl, each is optionally substituted with one to four Z^1;

Y_1-V is N-CH_2, N-$CH(CH_3)$, N-CF_2, or CH-CH_2, CH-CF_2, CH-NH, N-S(O), N-$S(O)_2$, N-C(O), CH-C(O) or cyclopropyl;

Y_2 is C, CH or N;

R^2 is H, C_{1-6} alkyl, C_{1-6} alkyl-alkoxy, -C_{1-6} alkyl-cycloalkoxy, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -OR^{2a}, -S-R^{2a}, -S(O)R^{2a}, -S(O)(NH)R^{2a}, -$S(O)_2R^{2a}$, -$S(O)_2N(R^{2a})(R^{2b})$, or -$S(O)(NR^{2a})R^{2b}$, wherein the alkyl, alkoxy, cycloalkoxy, haloalkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^1 and wherein any two Z_1 can be combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl or C_{6-10} aryl or 5-10 membered heteroaryl;

X is each independently -N=, -C(H)=, or -$C(R^8)$=;

each R^3 and $R^{3'}$is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -NO_2, -OR^{3a}, -C(O)R^{3a}, -CH_2C(O)OR^{3a}, -C(O)OR^{3a}, -C(O)$N(R^{3a})(R^{3b})$, -$N(R^{3a})$C(O)R^{3b}, -$N(R^{3a})$C(O)OR^{3b}, -$N(R^{3a})$C(O)$N(R^{3b})_2$, -C(O)$NHS(O)_2R^{3a}$, - C(O)$NR^{3a}S(O)_2R^{3b}$, -C(O)$NR^{3a}S(O)_2NR^{3b}R^{3c}$, -C(O)$NR^{3a}$-S(O)(=$NR^{3b}$)$R^{3c}$, -$S(O)_2R^{3a}$, -$S(O)_2OR^{3a}$, -$S(O)_2N(R^{3a})(R^{3b})$, -$N(R^{3a})S(O)_2R^{3b}$, -$S(O)_2NHC(O)R^{3a}$, -S(O)(=$NR^{3a}$)$R^{3b}$, -S(O)(=$NR^{3a}$)$NR^{3b}$, -S(=$NR^{3a}$)(=$NR^{3b}$)$R^{3c}$, -P(O)$(OR^{3a})(R^{3b})$, -P(O)$(OR^{3a})(OR^{3b})$, -$B(OR^{3a})(OR^{3b})$, or -O-$C_{1-6}$alkyl-C(O)$OR^{3a}$, wherein the alkyl, haloalkyl, alkenyl, alkynyl,

cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four R^{3d};

each R^{3a}, R^{3b}, and R^{3c} is independently H, C_{1-6} alkyl, C_{6-10} aryl, 5-10 membered heteroaryl, C_{1-6} haloalkyl, C_{2-8} alkoxyalkyl, -C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-$N(R^{9a})C(O)$-O-C_{1-4} alkyl-$OP(O)(OR^{9c})_2$, -C_{1-4} alkyl-$C(O)N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl- $OP(O)(OR^{9c})_2$, -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, - $CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, C_{1-6} alkyl-heterocyclyl, C_{1-6} alkyl- aryl or C_{1-6} alkyl-(5-10 membered) heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each R^{5a} and R^{5b} is independently H, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, -C_{1-6} alkyl-$N(R^{9a})(R^{9b})$, -CN, $-OR^{5a1}$, or $-N(R^{5a1})(R^{5a2})$; or R^{5a} and R^{5b} are combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{5a3};each R^{5a1} and R^{5a2} is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, herein the cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four halogen;

each R^{3d} and R^{5a3} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, or -$C(O)N(R^{2a})(R^{2b})$, wherein the heterocyclyl or 5-10 membered heteroaryl in each instance is optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

each R^8 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, $-NH_2$, $-N_3$, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$;

each R^{9a} and R^{9b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, $-O-R^{12a}$, $-C(O)R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})$-$C(O)R^{12b}$, $-N(R^{12a})C(O)O(R^{12b})$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-N(R^{12a})S(O)_2$-$N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, -OC(O)-$N(R^{12a})(R^{12b})$, -S-R^{12a}, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or -$Si(R^{12a})_3$; or R^{9a} and R^{9b} together form a 3-10 membered heterocyclyl optionally substituted

with C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, $-O-R^{12a}$, $-C(O)R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})-C(O)R^{12b}$, $-N(R^{12a})C(O)O(R^{12b})$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-N(R^{12a})S(O)_2-N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or $-Si(R^{12a})_3$;

each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, $-N_3$, -CN, $-O-R^{12a}$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1a};

each Z^{1a} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, $-O-R^{12a}$, $-C(O)R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})-C(O)R^{12b}$, $-N(R^{12a})C(O)O(R^{12b})$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-N(R^{12a})S(O)_2-N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or $-Si(R^{12a})_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each Z^{1b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, $-NH_2$, $-N_3$, -SH, $-O(C_{1-9}$ alkyl), $-O(C_{1-8}$ haloalkyl), $-O(C_{2-6}$ alkenyl), $-O(C_{2-6}$ alkynyl), $-O(C_{3-15}$ cycloalkyl), -O(heterocyclyl), $-O(C_{6-10}$ aryl), -O(5-10 membered heteroaryl), $-NH(C_{1-9}$ alkyl), $-NH(C_{1-8}$ haloalkyl), $-NH(C_{2-6}$ alkenyl), $-NH(C_{2-6}$ alkynyl), $-NH(C_{3-15}$ cycloalkyl), -NH(heterocyclyl), $-NH(C_{6-10}$ aryl), -NH(5-10 membered heteroaryl), -N(cyclo-alkyl), $-N(C_{1-9}$ alkyl)$_2$, $-N(C_{1-8}$ haloalkyl)$_2$, $-N(C_{2-6}$ alkenyl)$_2$, $-N(C_{2-6}$ alkynyl)$_2$, $-N(C_{3-15}$ cycloalkyl)$_2$, -N(heterocyclyl)$_2$, $-N(C_{6-10}$ aryl)$_2$, -N(5-10 membered heteroaryl)$_2$, $-N(C_{1-9}$ alkyl)$(C_{1-8}$ haloalkyl), $-N(C_{1-9}$ alkyl)$(C_{2-6}$ alkenyl), $-N(C_{1-9}$ alkyl)$(C_{2-6}$ alkynyl), $-N(C_{1-9}$ alkyl)$(C_{3-15}$ cycloalkyl), -N(C_{1-9} alkyl)(heterocyclyl), $-N(C_{1-9}$ alkyl)$(C_{6-10}$ aryl), $-N(C_{1-9}$ alkyl)(5-10 membered heteroaryl), $-C(O)(C_{1-9}$ alkyl), $-C(O)(C_{1-8}$ haloalkyl), $-C(O)(C_{2-6}$ alkenyl), $-C(O)(C_{2-6}$ alkynyl), $-C(O)(C_{3-15}$ cycloalkyl), -C(O)(heterocyclyl), $-C(O)(C_{6-10}$ aryl), -C(O)(5-10 membered heteroaryl), $-C(O)O(C_{1-9}$ alkyl), $-C(O)O(C_{1-8}$ haloalkyl), $-C(O)O(C_{2-6}$

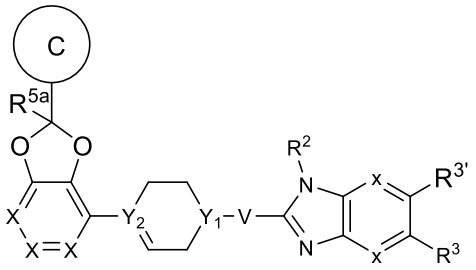
alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(5-10 membered heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(5-10 membered heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(5-10 membered heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl),-NHC(O)O(C_{6-10} aryl), -NHC(O)O(5-10 membered heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), or -NHC(O)NH(5-10 membered heteroaryl), wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H,-O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(5-10 membered heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(5-10 membered heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(5-10 membered heteroaryl), or -NHC(O)NH(C_{1-9} alkyl);

each R^{1b}, R^{1c}, R^{2a}, R^{2b}, R^{4c}, R^{9c}, R^{12a}, R^{12b}, and R^{12c} is independently H, -OH, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; and

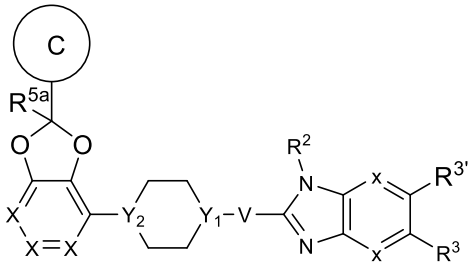
each R^{3e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, -C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C(O)N(R^{9a})(R^{9b}), -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; wherein each 5-10 membered heteroaryl has 5 to 12 ring members and

has one to four heteroatoms, each is independently N, O, or S; and wherein each heterocyclyl has 3 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S.

3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is a compound of Formula I-A-4 or Formula I-A-5



(I-A-4)



(I-A-5)

, wherein

Ring C is C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl or 5-10 membered heteroaryl, which is each optionally substituted with one to four Z^1;

Y_1-V is N-CH_2, N-$CH(CH_3)$, N-CF_2, CH-CH_2, CH-CF_2, CH-NH, N-S(O), N-$S(O)_2$, N-C(O), CH-C(O) or cyclopropyl;

Y_2 is C, CH or N;

R^2 is H, C_{1-6} alkyl, C_{1-6} alkyl-alkoxy, C_{1-6} alkyl-cycloalkoxy, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, $-OR^{2a}$, $-S-R^{2a}$, $-S(O)R^{2a}$, $-S(O)(NH)R^{2a}$, $-S(O)_2R^{2a}$, $-S(O)_2N(R^{2a})(R^{2b})$, or $-S(O)(NR^{2a})R^{2b}$, wherein the alkyl, alkoxy, cycloalkoxy, haloalkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl is each optionally substituted with one to four Z^1 and wherein any two Z_1 can be combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl or C_{6-10} aryl or 5-10 membered heteroaryl;

X is each independently -N=, -C(H)=, or $-C(R^8)=$;

each R^3 and $R^{3'}$ is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -

NO_2, -OR^{3a}, -$C(O)R^{3a}$, -$CH_2C(O)OR^{3a}$, -$C(O)OR^{3a}$, -$C(O)N(R^{3a})(R^{3b})$, -$N(R^{3a})C(O)R^{3b}$, -$N(R^{3a})C(O)OR^{3b}$, -$N(R^{3a})C(O)N(R^{3b})_2$, -$C(O)NHS(O)_2R^{3a}$, - $C(O)NR^{3a}S(O)_2R^{3b}$, - $C(O)NR^{3a}S(O)_2NR^{3b}R^{3c}$, -$C(O)NR^{3a}$-$S(O)(=NR^{3b})R^{3c}$, -$S(O)_2R^{3a}$, -$S(O)_2OR^{3a}$, -$S(O)_2N(R^{3a})(R^{3b})$, -$N(R^{3a})S(O)_2R^{3b}$, -$S(O)_2NHC(O)R^{3a}$, -$S(O)(=NR^{3a})R^{3b}$, -$S(O)(=NR^{3a})NR^{3b}$, -$S(=NR^{3a})(=NR^{3b})R^{3c}$, -$P(O)(OR^{3a})(R^{3b})$, -$P(O)(OR^{3a})(OR^{3b})$, -$B(OR^{3a})(OR^{3b})$, or -O-$C_{1-6}$alkyl-$C(O)OR^{3a}$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four R^{3d};

each R^{3a}, R^{3b}, and R^{3c} is independently H, C_{1-6} alkyl, C_{6-10} aryl, 5-10 membered heteroaryl, C_{1-6} haloalkyl, C_{2-8} alkoxyalkyl, -C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-$N(R^{9a})C(O)$-O-C_{1-4} alkyl-$OP(O)(OR^{9c})_2$, -C_{1-4} alkyl-$C(O)N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl- $OP(O)(OR^{9c})_2$, -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, - $CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, C_{1-6} alkyl-heterocyclyl, C_{1-6} alkyl- aryl or C_{1-6} alkyl-(5-10 membered) heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each R^{5a} is independently H, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, -C_{1-6} alkyl-$N(R^{9a})(R^{9b})$, -CN, -OR^{5a1}, or -$N(R^{5a1})(R^{5a2})$;

each R^{5a1} and R^{5a2} is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four halogen;

each R^{3d} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, or -$C(O)N(R^{2a})(R^{2b})$, wherein the heterocyclyl or 5-10 membered heteroaryl is optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

each R^8 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$;

each R^{9a} and R^{9b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -$C(O)R^{12a}$,

-C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$; or R^{9a} and R^{9b} together form a 3-10 membered heterocyclyl optionally substituted with C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$;

each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -N_3, -CN, or -O-R^{12a}, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1a};

each Z^{1a} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

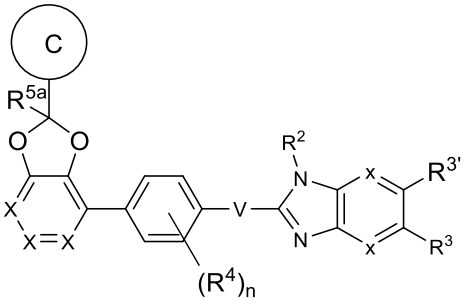
each Z^{1b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, -NO_2, -NH_2, -N_3, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{2-6} alkenyl), -O(C_{2-6} alkynyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(C_{6-10} aryl), -O(5-10 membered heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{2-6} alkenyl), -NH(C_{2-6} alkynyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(C_{6-10} aryl), -NH(5-10 membered heteroaryl), -N(cyclo-alkyl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$, -N(C_{2-6} alkenyl)$_2$, -N(C_{2-6} alkynyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -N(heterocyclyl)$_2$, -N(C_{6-10} aryl)$_2$, -N(5-10 membered heteroaryl)$_2$, -

N(C_{1-9} alkyl)(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)(C_{2-6} alkenyl), -N(C_{1-9} alkyl)(C_{2-6} alkynyl), -N(C_{1-9} alkyl)(C_{3-15} cycloalkyl), -N(C_{1-9} alkyl)(heterocyclyl), -N(C_{1-9} alkyl)(C_{6-10} aryl), -N(C_{1-9} alkyl)(5-10 membered heteroaryl), -C(O)(C_{1-9} alkyl), -C(O)(C_{1-8} haloalkyl), -C(O)(C_{2-6} alkenyl), -C(O)(C_{2-6} alkynyl), -C(O)(C_{3-15} cycloalkyl), -C(O)(heterocyclyl), -C(O)(C_{6-10} aryl), -C(O)(5-10 membered heteroaryl), -C(O)O(C_{1-9} alkyl), -C(O)O(C_{1-8} haloalkyl), -C(O)O(C_{2-6} alkenyl), -C(O)O(C_{2-6} alkynyl), -C(O)O(C_{3-15} cycloalkyl), -C(O)O(heterocyclyl), -C(O)O(C_{6-10} aryl), -C(O)O(5-10 membered heteroaryl), -C(O)NH_2, -C(O)NH(C_{1-9} alkyl), -C(O)NH(C_{1-8} haloalkyl), -C(O)NH(C_{2-6} alkenyl), -C(O)NH(C_{2-6} alkynyl), -C(O)NH(C_{3-15} cycloalkyl), -C(O)NH(heterocyclyl), -C(O)NH(C_{6-10} aryl), -C(O)NH(5-10 membered heteroaryl), -C(O)N(C_{1-9} alkyl)$_2$, -C(O)N(C_{1-8} haloalkyl)$_2$, -C(O)N(C_{2-6} alkenyl)$_2$, -C(O)N(C_{2-6} alkynyl)$_2$, -C(O)N(C_{3-15} cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, -C(O)N(C_{6-10} aryl)$_2$, -C(O)N(5-10 membered heteroaryl)$_2$, -NHC(O)(C_{1-9} alkyl), -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{2-6} alkenyl), -NHC(O)(C_{2-6} alkynyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(C_{6-10} aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkenyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl),-NHC(O)O(C_{6-10} aryl), -NHC(O)O(5-10 membered heteroaryl), -NHC(O)NH(C_{1-9} alkyl), -NHC(O)NH(C_{1-8} haloalkyl), -NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), or -NHC(O)NH(5-10 membered heteroaryl), wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, -NH_2, CO_2H,-O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(5-10 membered heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(5-10 membered heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(5-10 membered heteroaryl), or -NHC(O)NH(C_{1-9} alkyl);

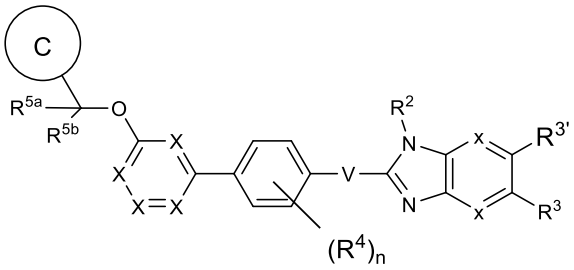
each R^{1b}, R^{1c}, R^{2a}, R^{2b}, R^{4c}, R^{9c}, R^{12a}, R^{12b}, and R^{12c} is independently H, -OH, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; and

each R^{3e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, -C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C(O)N(R^{9a})(R^{9b}), -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; wherein each 5-10 membered heteroaryl has 5 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S; and wherein each heterocyclyl has 3 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S.

4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is a compound of Formula I-A-6 or Formula I-A-7



(I-A-6)



(I-A-7)

, wherein

Ring C is C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl or 5-10 membered heteroaryl, which is each optionally substituted with one to four Z^1;

V is CH_2, $CH(CH_3)$, NH, C(O),S(O),$S(O)_2$;

n=0, 1, 2, 3, or 4;

R^2 is H, C_{1-6} alkyl, -C_{1-6} alkyl-alkoxy, -C_{1-6} alkyl-cycloalkoxy, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -OR^{2a}, -S-R^{2a}, -S(O)R^{2a}, -S(O)(NH)R^{2a}, -$S(O)_2R^{2a}$, -$S(O)_2N(R^{2a})(R^{2b})$, or -S(O)(NR^{2a})R^{2b}, wherein the alkyl, alkoxy, cycloalkoxy, haloalkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four

Z^1 and wherein any two Z_1 can be combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl or C_{6-10} aryl or 5-10 membered heteroaryl;

X is each independently -N=, -C(H)=, or -C(R^8)=;

each R^3 and $R^{3'}$is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, -CN, -NO_2, -OR^{3a}, -$C(O)R^{3a}$, -$CH_2C(O)OR^{3a}$, -$C(O)OR^{3a}$, -$C(O)N(R^{3a})(R^{3b})$, -$N(R^{3a})C(O)R^{3b}$, -$N(R^{3a})C(O)OR^{3b}$, -$N(R^{3a})C(O)N(R^{3b})_2$, -$C(O)NHS(O)_2R^{3a}$, - $C(O)NR^{3a}S(O)_2R^{3b}$, -$C(O)NR^{3a}S(O)_2NR^{3b}R^{3c}$, -$C(O)NR^{3a}$-$S(O)(=NR^{3b})R^{3c}$, -$S(O)_2R^{3a}$, -$S(O)_2OR^{3a}$, -$S(O)_2N(R^{3a})(R^{3b})$, -$N(R^{3a})S(O)_2R^{3b}$, -$S(O)_2NHC(O)R^{3a}$, -$S(O)(=NR^{3a})R^{3b}$, -$S(O)(=NR^{3a})NR^{3b}$, -$S(=NR^{3a})(=NR^{3b})R^{3c}$, -$P(O)(OR^{3a})(R^{3b})$, -$P(O)(OR^{3a})(OR^{3b})$, -$B(OR^{3a})(OR^{3b})$, or -O-$C_{1-6}$alkyl-$C(O)OR^{3a}$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four R^{3d};

each R^{3a}, R^{3b}, and R^{3c} is independently H, C_{1-6} alkyl, C_{6-10} aryl, 5-10 membered heteroaryl, C_{1-6} haloalkyl, C_{2-8} alkoxyalkyl, -C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-$N(R^{9a})C(O)$-O-C_{1-4} alkyl-$OP(O)(OR^{9c})_2$, -C_{1-4} alkyl-$C(O)N(R^{9a})(R^{9b})$, -C1-4 alkyl-O-C(O)-O-C1-4 alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl- $OP(O)(OR^{9c})_2$, -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, - $CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, C_{1-6} alkyl-heterocyclyl, C_{1-6} alkyl- aryl or C_{1-6} alkyl-(5-10 membered) heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each R^4 is independently H, CH_2OH, -OH, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -CN, -N_3, -O-R^{4a}, -$C(O)R^{4a}$, -C(O)O-R^{4a}, -$C(O)N(R^{4a})(R^{4b})$, -$N(R^{4a})(R^{4b})$, -$N(R^{4a})_2(R^{4b})^+$, -$N(R^{4a})$-$C(O)R^{4b}$, -$N(R^{4a})C(O)O(R^{4b})$, -$N(R^{4a})C(O)N(R^{4b})(R^{4c})$, -$N(R^{4a})S(O)_2(R^{4b})$, -$N(R^{4a})S(O)_2$-$N(R^{4b})(R^{4c})$, -$N(R^{4a})S(O)_2O(R^{4b})$, -$OC(O)R^{4a}$, -$OC(O)OR^{4a}$, -OC(O)-$N(R^{4a})(R^{4b})$, -S-$R^{4a}$, -$S(O)R^{4a}$, -$S(O)(NH)R^{4a}$, -$S(O)_2R^{4a}$, -$S(O)_2N(R^{4a})(R^{4b})$, -$S(O)(NR^{4a})R^{4b}$, or -$Si(R^{4a})_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; or two R^4 groups attached to adjacent ring atoms are combined with the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four Z^{1b};

each R^{5a} and R^{5b} is independently H, C_{1-6} alkyl, C_{1-6} alkyloxy, C_{1-6} haloalkyl, C_{2-6} alkoxyalkyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, -C_{1-6} alkyl-$N(R^{9a})(R^{9b})$, -CN, -OR^{5a1}, or

-N(R^{5a1})(R^{5a2}); or R^{5a} and R^{5b} are combined with the atoms to which they are attached to form a C_{3-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four R^{5a3};

each R^{5a1} and R^{5a2} is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four halogen;

each R^{3d} and R^{5a3} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, or -C(O)N(R^{2a})(R^{2b}), wherein the heterocyclyl or 5-10 membered heteroaryl in each instance is optionally substituted with C_{1-6} alkyl, C_{1-6} haloalkyl, or C_{1-6} haloalkoxy;

each R^8 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, $-NH_2$, $-N_3$, -SH, -O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -N(C_{1-9} alkyl)$_2$, -N(C_{1-8} haloalkyl)$_2$;

each R^{9a} and R^{9b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$; or R^{9a} and R^{9b} together form a 3-10 membered heterocyclyl optionally substituted with C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, -O-R^{12a}, -C(O)R^{12a}, -C(O)O-R^{12a}, -C(O)N(R^{12a})(R^{12b}), -N(R^{12a})(R^{12b}), -N(R^{12a})$_2$(R^{12b})$^+$, -N(R^{12a})-C(O)R^{12b}, -N(R^{12a})C(O)O(R^{12b}), -N(R^{12a})C(O)N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$(R^{12b}), -N(R^{12a})S(O)$_2$-N(R^{12b})(R^{12c}), -N(R^{12a})S(O)$_2$O(R^{12b}), -OC(O)R^{12a}, -OC(O)OR^{12a}, -OC(O)-N(R^{12a})(R^{12b}), -S-R^{12a}, -S(O)R^{12a}, -S(O)(NH)R^{12a}, -S(O)$_2$$R^{12a}$, -S(O)$_2$N($R^{12a}$)($R^{12b}$), -S(O)(N$R^{12a}$)$R^{12b}$, or -Si($R^{12a}$)$_3$;

each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, $-N_3$, -CN, or -O-R^{12a}, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1a};

each Z^{1a} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, $-NO_2$, -CN, $-N_3$, $-O-R^{12a}$, $-C(O)R^{12a}$, $-C(O)O-R^{12a}$, $-C(O)N(R^{12a})(R^{12b})$, $-N(R^{12a})(R^{12b})$, $-N(R^{12a})_2(R^{12b})^+$, $-N(R^{12a})-C(O)R^{12b}$, $-N(R^{12a})C(O)O(R^{12b})$, $-N(R^{12a})C(O)N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2(R^{12b})$, $-N(R^{12a})S(O)_2-N(R^{12b})(R^{12c})$, $-N(R^{12a})S(O)_2O(R^{12b})$, $-OC(O)R^{12a}$, $-OC(O)OR^{12a}$, $-OC(O)-N(R^{12a})(R^{12b})$, $-S-R^{12a}$, $-S(O)R^{12a}$, $-S(O)(NH)R^{12a}$, $-S(O)_2R^{12a}$, $-S(O)_2N(R^{12a})(R^{12b})$, $-S(O)(NR^{12a})R^{12b}$, or $-Si(R^{12a})_3$, wherein the alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

each Z^{1b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -OH, -CN, CO_2R^{3e}, $-NO_2$, $-NH_2$, $-N_3$, -SH, $-O(C_{1-9}$ alkyl), $-O(C_{1-8}$ haloalkyl), $-O(C_{2-6}$ alkenyl), $-O(C_{2-6}$ alkynyl), $-O(C_{3-15}$ cycloalkyl), -O(heterocyclyl), $-O(C_{6-10}$ aryl), -O(5-10 membered heteroaryl), $-NH(C_{1-9}$ alkyl), $-NH(C_{1-8}$ haloalkyl), $-NH(C_{2-6}$ alkenyl), $-NH(C_{2-6}$ alkynyl), $-NH(C_{3-15}$ cycloalkyl), -NH(heterocyclyl), $-NH(C_{6-10}$ aryl), -NH(5-10 membered heteroaryl), -N(cyclo-alkyl), $-N(C_{1-9}$ alkyl)$_2$, $-N(C_{1-8}$ haloalkyl)$_2$, $-N(C_{2-6}$ alkenyl)$_2$, $-N(C_{2-6}$ alkynyl)$_2$, $-N(C_{3-15}$ cycloalkyl)$_2$, -N(heterocyclyl)$_2$, $-N(C_{6-10}$ aryl)$_2$, -N(5-10 membered heteroaryl)$_2$, $-N(C_{1-9}$ alkyl)$(C_{1-8}$ haloalkyl), $-N(C_{1-9}$ alkyl)$(C_{2-6}$ alkenyl), $-N(C_{1-9}$ alkyl)$(C_{2-6}$ alkynyl), $-N(C_{1-9}$ alkyl)$(C_{3-15}$ cycloalkyl), $-N(C_{1-9}$ alkyl)(heterocyclyl), $-N(C_{1-9}$ alkyl)$(C_{6-10}$ aryl), $-N(C_{1-9}$ alkyl)(5-10 membered heteroaryl), $-C(O)(C_{1-9}$ alkyl), $-C(O)(C_{1-8}$ haloalkyl), $-C(O)(C_{2-6}$ alkenyl), $-C(O)(C_{2-6}$ alkynyl), $-C(O)(C_{3-15}$ cycloalkyl), -C(O)(heterocyclyl), $-C(O)(C_{6-10}$ aryl), -C(O)(5-10 membered heteroaryl), $-C(O)O(C_{1-9}$ alkyl), $-C(O)O(C_{1-8}$ haloalkyl), $-C(O)O(C_{2-6}$ alkenyl), $-C(O)O(C_{2-6}$ alkynyl), $-C(O)O(C_{3-15}$ cycloalkyl), -C(O)O(heterocyclyl), $-C(O)O(C_{6-10}$ aryl), -C(O)O(5-10 membered heteroaryl), $-C(O)NH_2$, $-C(O)NH(C_{1-9}$ alkyl), $-C(O)NH(C_{1-8}$ haloalkyl), $-C(O)NH(C_{2-6}$ alkenyl), $-C(O)NH(C_{2-6}$ alkynyl), $-C(O)NH(C_{3-15}$ cycloalkyl), -C(O)NH(heterocyclyl), $-C(O)NH(C_{6-10}$ aryl), -C(O)NH(5-10 membered heteroaryl), $-C(O)N(C_{1-9}$ alkyl)$_2$, $-C(O)N(C_{1-8}$ haloalkyl)$_2$, $-C(O)N(C_{2-6}$ alkenyl)$_2$, $-C(O)N(C_{2-6}$ alkynyl)$_2$, $-C(O)N(C_{3-15}$ cycloalkyl)$_2$, -C(O)N(heterocyclyl)$_2$, $-C(O)N(C_{6-10}$ aryl)$_2$, -C(O)N(5-10 membered heteroaryl)$_2$, $-NHC(O)(C_{1-9}$ alkyl), $-NHC(O)(C_{1-8}$ haloalkyl), $-NHC(O)(C_{2-6}$ alkenyl), $-NHC(O)(C_{2-6}$ alkynyl), $-NHC(O)(C_{3-15}$ cycloalkyl), -NHC(O)(heterocyclyl), $-NHC(O)(C_{6-10}$ aryl), -NHC(O)(5-10 membered heteroaryl), $-NHC(O)O(C_{1-9}$ alkyl), $-NHC(O)O(C_{1-8}$ haloalkyl), $-NHC(O)O(C_{2-6}$ alkenyl), $-NHC(O)O(C_{2-6}$ alkynyl), $-NHC(O)O(C_{3-15}$ cycloalkyl), -NHC(O)O(heterocyclyl),$-NHC(O)O(C_{6-10}$ aryl), -NHC(O)O(5-10 membered heteroaryl), $-NHC(O)NH(C_{1-9}$ alkyl), $-NHC(O)NH(C_{1-8}$ haloalkyl), -

NHC(O)NH(C_{2-6} alkenyl), -NHC(O)NH(C_{2-6} alkynyl), -NHC(O)NH(C_{3-15} cycloalkyl), -NHC(O)NH(heterocyclyl), -NHC(O)NH(C_{6-10} aryl), or -NHC(O)NH(5-10 membered heteroaryl), wherein the alkyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to three C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -OH, $-NH_2$, CO_2H,-O(C_{1-9} alkyl), -O(C_{1-8} haloalkyl), -O(C_{3-15} cycloalkyl), -O(heterocyclyl), -O(aryl), -O(5-10 membered heteroaryl), -NH(C_{1-9} alkyl), -NH(C_{1-8} haloalkyl), -NH(C_{3-15} cycloalkyl), -NH(heterocyclyl), -NH(aryl), -NH(5-10 membered heteroaryl), -N(C_{1-9} alkyl)$_2$, -N(C_{3-15} cycloalkyl)$_2$, -NHC(O)(C_{1-8} haloalkyl), -NHC(O)(C_{3-15} cycloalkyl), -NHC(O)(heterocyclyl), -NHC(O)(aryl), -NHC(O)(5-10 membered heteroaryl), -NHC(O)O(C_{1-9} alkyl), -NHC(O)O(C_{1-8} haloalkyl), -NHC(O)O(C_{2-6} alkynyl), -NHC(O)O(C_{3-15} cycloalkyl), -NHC(O)O(heterocyclyl), -NHC(O)O(aryl), -NHC(O)O(5-10 membered heteroaryl), or -NHC(O)NH(C_{1-9} alkyl;

each R^{1b}, R^{1c}, R^{2a}, R^{2b}, R^{4a}, R^{4b}, R^{4c}, R^{9c}, R^{12a}, R^{12b}, and R^{12c} is independently H, -OH, C_{1-9} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b}; and

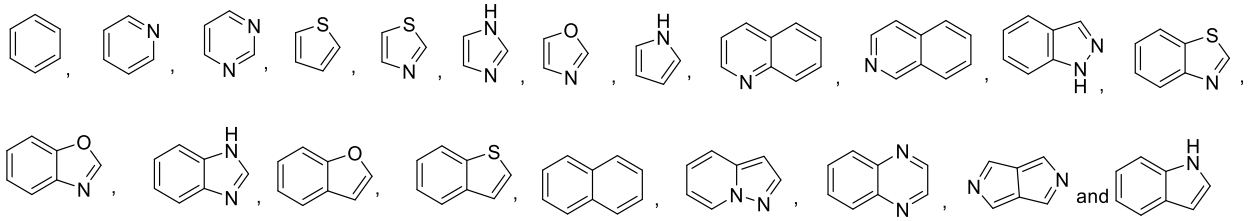
each R^{3e} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, -C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C(O)N(R^{9a})(R^{9b}), -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-N(R^{9a})(R^{9b}), -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

wherein each 5-10 membered heteroaryl has 5 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S;

and wherein each heterocyclyl has 3 to 12 ring members and has one to four heteroatoms, each is independently N, O, or S.

5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein each R^{5a} and R^{5b}, if present, is independently H, C_{1-9} alkyl, or C_{2-6} alkoxyalkyl and wherein the C_{1-9} alkyl or C_{2-6} alkoxyalkyl in each instance is optionally substituted with one or more halogens;

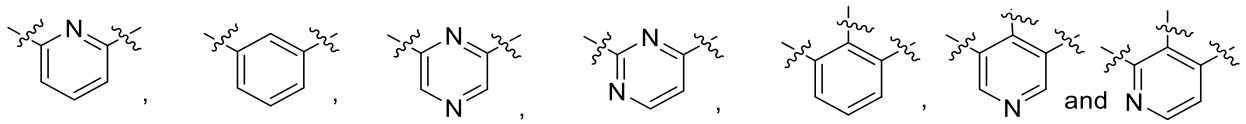
preferably, wherein Ring C is C_{6-10} aryl or 5-10 membered heteroaryl selected from the group consisting of



which is each optionally substituted with one to four substituents, each independently selected from the group consisting of H, OH, oxo, halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, $-NO_2$, $-N_3$, -CN, $-O-C_{1-6}$ alkyl, $-C(O)-C_{1-6}$ alkyl, $-C(O)-N(C_{0-6}$ alkyl$)(C_{0-6}$ alkyl), and $-N(C_{0-6}$ alkyl$)(C_{0-6}$ alkyl),

wherein the one to four substituents in each instance is optionally substituted with one or more halogens;

preferably, wherein Ring A is selected from the group consisting of

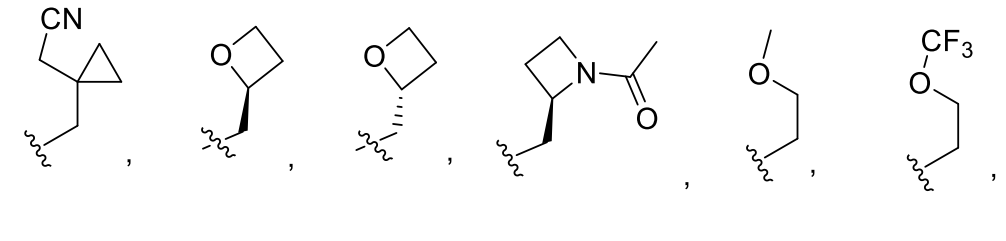


which is each optionally substituted with one to four Z^{1a};

preferably, wherein each of the one to four Z^{1a} is independently H, halogen, C_{1-9} alkyl, C_{1-6} alkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-15} cycloalkyl, or heterocyclyl, which is each optionally substituted with one or more halogens;

preferably, wherein R^2 is C_{1-6} alkyl, C_{1-6} alkyl-alkoxy, C_{1-6} alkyl-cycloalkoxy, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, or 5-10 membered heteroaryl, which is each optionally substituted with one to four Z^1;

preferably, wherein R^2 is selected from the group consisting of



which is each optionally substituted with one to four Z^1;

preferably, wherein $R^{2'}$ is H, C_{1-6} alkyl, C_{1-6} haloalkyl, or -C_{1-6} alkyl–cycloalkoxy, which is each optionally substituted with one or more halogens;

preferably, wherein each R^3 and $R^{3'}$ is independently H, C_{6-10} aryl, 5-10 membered heteroaryl, -$C(O)R^{3a}$, -$CH_2C(O)OR^{3a}$, -$C(O)N(R^{3a})(R^{3b})$, -$N(R^{3a})C(O)R^{3b}$, -$N(R^{3a})C(O)OR^{3b}$, -$N(R^{3a})C(O)N(R^{3b})_2$, -$C(O)NHS(O)_2R^{3a}$, - $C(O)NR^{3a}S(O)_2R^{3b}$, -$C(O)NR^{3a}S(O)_2NR^{3b}R^{3c}$, -$C(O)NR^{3a}$-$S(O)(=NR^{3b})R^{3c}$, -$S(O)_2N(R^{3a})(R^{3b})$, -$N(R^{3a})S(O)_2R^{3b}$, -$S(O)_2NHC(O)R^{3a}$, or -O-$C_{1-6}$alkyl-$C(O)OR^{3a}$, which is each optionally substituted with one to four R^{3d};

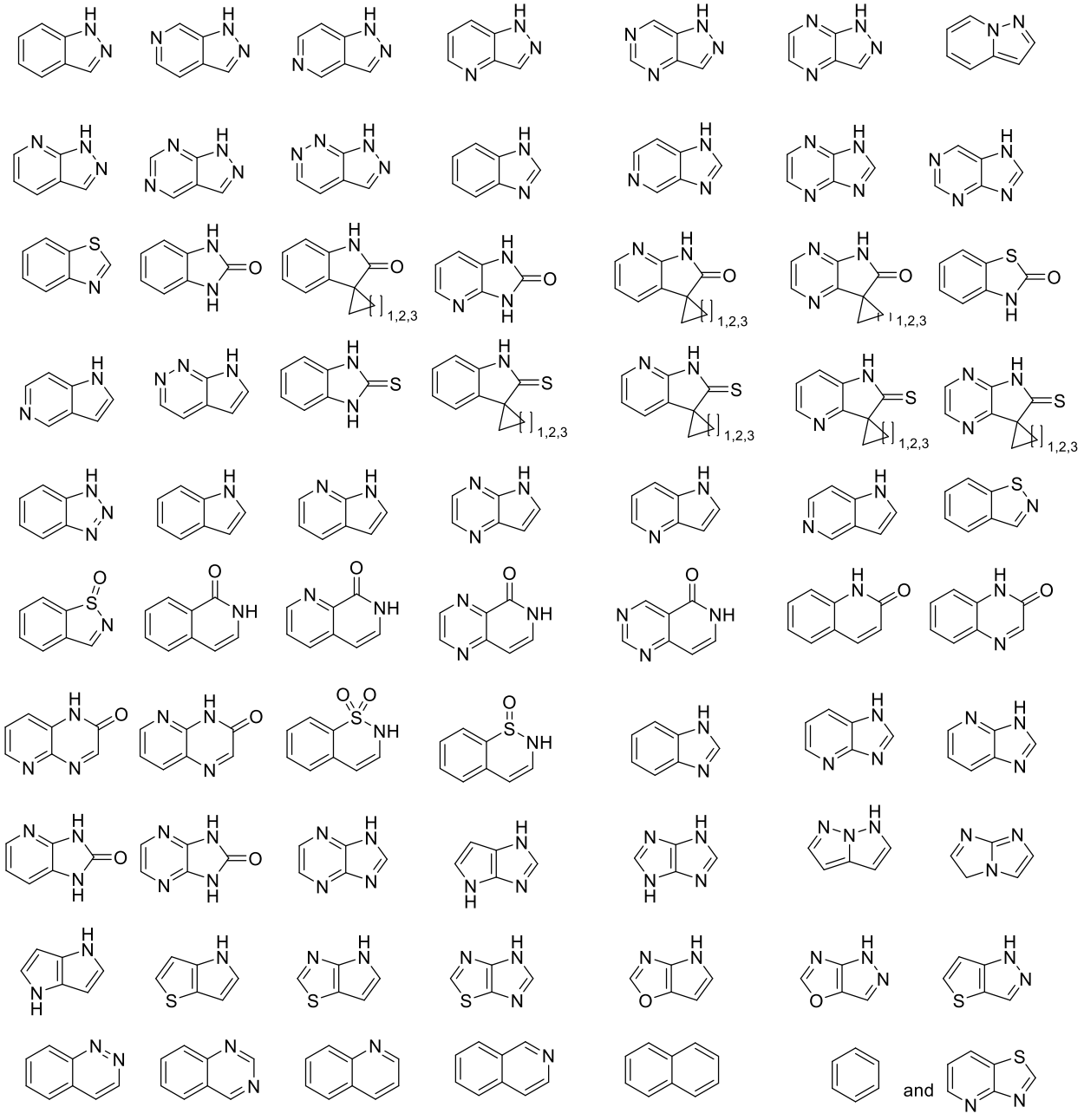
preferably, wherein each R^3 and $R^{3'}$ is independently H, $C(O)NR^{3a}(CH_2)_mR^{3b}$, $C(O)NR^{3a}(CH_2)_mC(O)R^{3b}$, $NR^{3a}C(O)(CH_2)_mR^{3b}$, $NR^{3a}(CH_2)_mR^{3b}$, $NR^{3a}(CH_2)_mC(O)R^{3b}$, $C(O)NR^{3a}R^{3b}$, or $NR^{3a}C(O)R^{3b}$, which is each optionally substituted with one to four R^{3d}, wherein m=0, 1, 2, or 3;

preferably, wherein each R^3 and $R^{3'}$ is independently H, $C(O)NHR^{3b}$, or $NHC(O)R^{3b}$;

preferably, wherein each R^{3b} is independently H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-8} alkoxyalkyl, -C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-$C(O)N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-O-C(O)-O-C_{1-4} alkyl, -C_{1-4} alkyl-O-C(O)-C_{1-4} alkyl-$N(R^{9a})(R^{9b})$, -C_{1-4} alkyl-C_{3-8} cycloalkyl, -C_{1-4} alkyl-heterocyclyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, - $CH_2CH(N(R^{9a})_2)C(O)OR^{9b}$, C1-6 alkyl-heterocyclyl, C1-6 alkyl-aryl or C1-6 alkyl-(5-10 membered) heteroaryl, wherein the alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, or 5-10 membered heteroaryl in each instance is optionally substituted with one to four Z^{1b};

preferably, wherein each R^{3b} is independently C_{6-10} aryl or 5-10 membered heteroaryl, which in each instance is optionally substituted with one to five R^{3f}, wherein R^{3f} is H, OH, oxo, NH_2, halogen, -NO_2, -N_3, -CN, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-10} cycloalkyl, heterocyclyl, -O-C_{1-6} alkyl, -C(O)-C_{1-6} alkyl, -$C(O)$-$N(R^{12a})(R^{12b})$, -$N(R^{12a})(R^{12b})$, C6-10 aryl, or 5-10 membered heteroaryl, wherein R^{3f} in each instance is optionally substituted with one or more halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, or C_{1-6} haloalkoxy;

preferably, wherein the aryl or 5-10 membered heteroaryl in R^{3b} is selected from the group consisting of:



, which is each optionally substituted with one to five R^{3f}.

6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein each R^4 is independently H, -OH, -CH_2OH, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -CN, -N_3, -O- C_{1-9} alkyl, or -C(O) C_{1-9} alkyl, which is each optionally substituted with one to four Z^{1b},

wherein two R^4 groups attached to adjacent ring atoms may be combined with the atoms to which they are attached to form a C_{5-10} cycloalkyl or heterocyclyl, which is each optionally substituted with one to four Z^{1b};

preferably, wherein each R^4 is independently H, halogen, -CH_2OH, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, or C_{3-15} cycloalkyl.

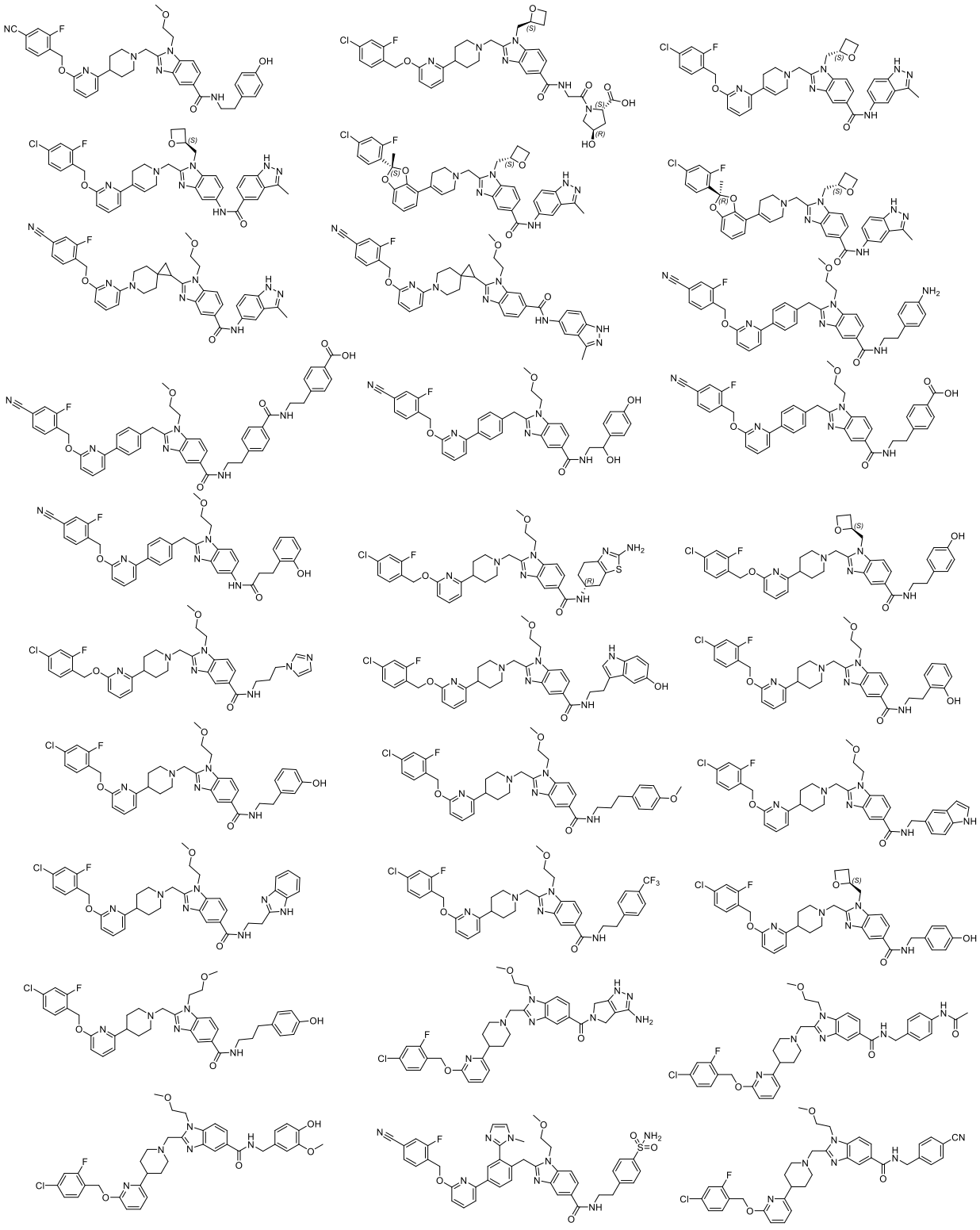
7. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt thereof, wherein each Z^1 is independently C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, halogen, C_{3-15} cycloalkyl, heterocyclyl, C_{6-10} aryl, 5-10 membered heteroaryl, oxo, -NO_2, -N_3, -CN, -O-R^{12a}, -C(O)-R^{12a}, -C(O)O-R^{12a}, -C(O)-N(R^{12a})(R^{12b}), or -N(R^{12a})(R^{12b});

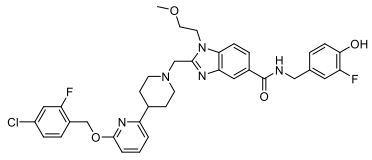
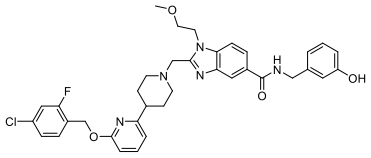
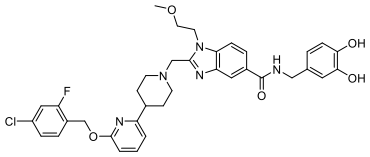
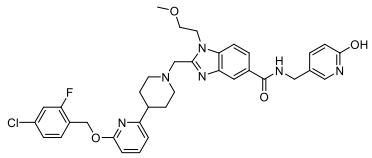
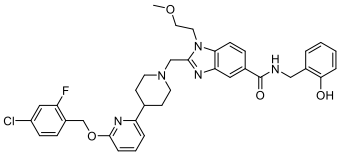
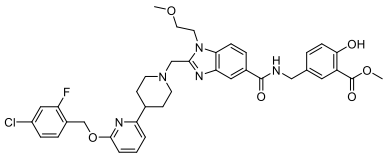
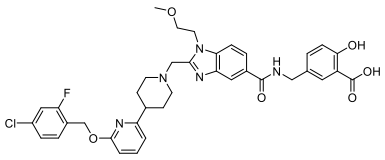
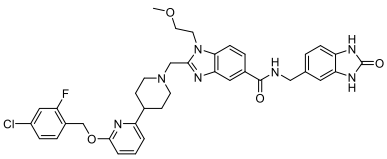
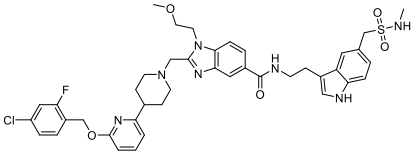
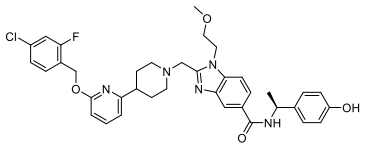
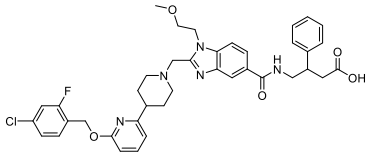
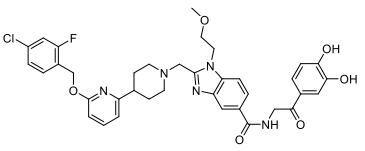
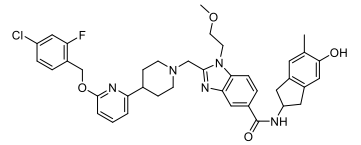
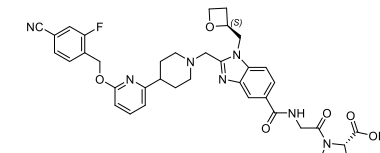
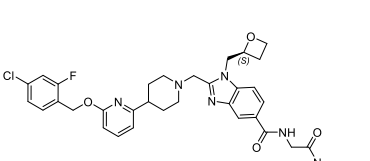
preferably, wherein each Z^{1a} is independently H, -OH, C_{1-9} alkyl, C_{1-8} haloalkyl, C_{1-6} alkoxy, C_{1-6} haloalkoxy, C_{2-6} alkoxyalkyl, or halogen;

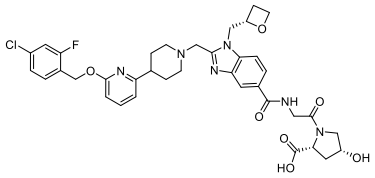
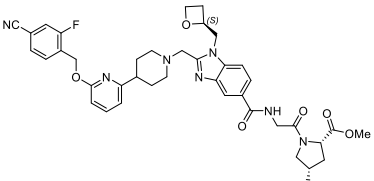
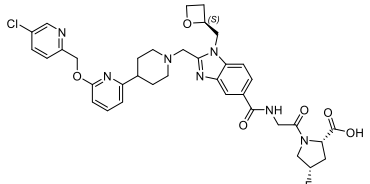
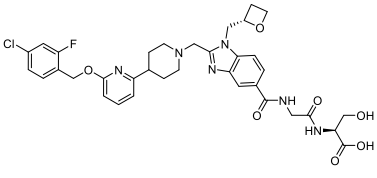
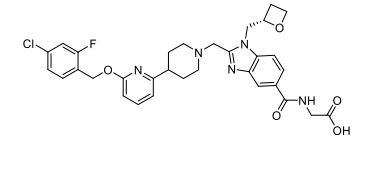
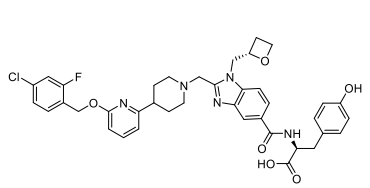
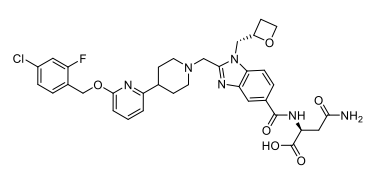
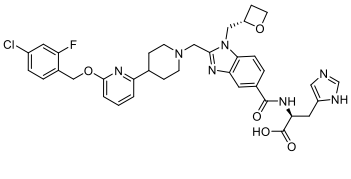
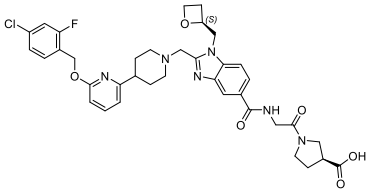
preferably, wherein each Z^{1b} is independently H, C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, oxo, -OH, or -CN;

preferably, wherein each R^8 is independently H, oxo, OH, C_{1-9} alkyl, C_{1-8} haloalkyl, halogen, -O(C_{1-3} alkyl), or -O(C_{1-3} haloalkyl).

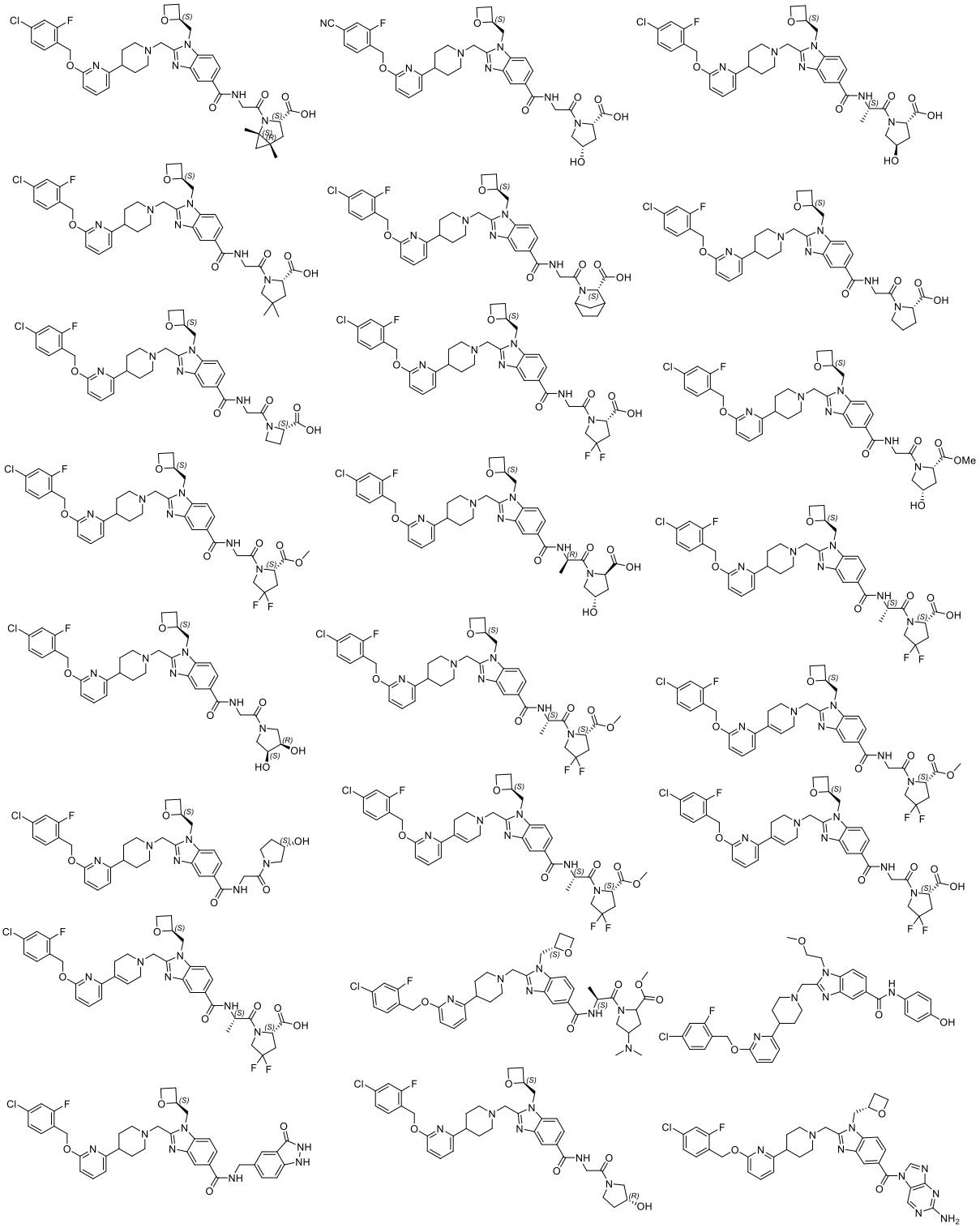
8. The compound of claim 1, or a pharmaceutically acceptable salt thereof, having a structure selected from the group consisting of

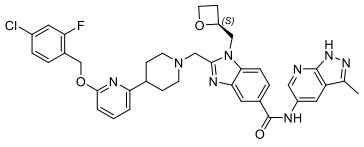
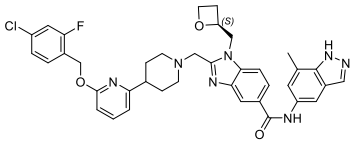
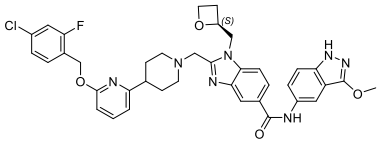
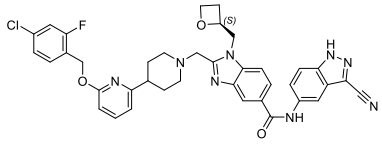
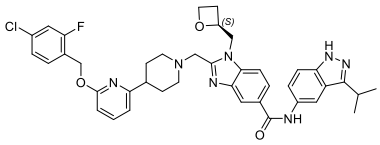
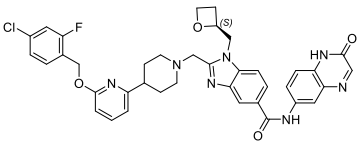
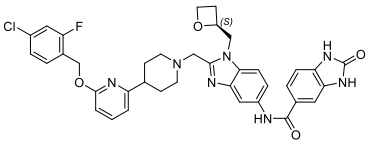
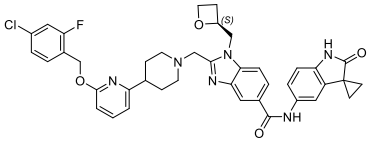
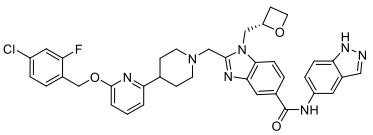
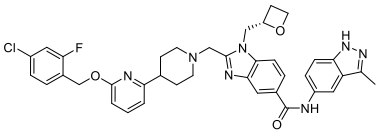
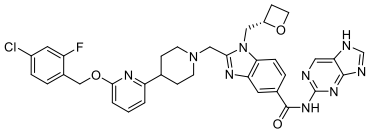
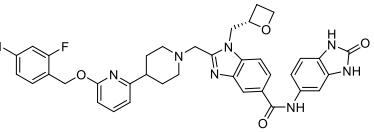
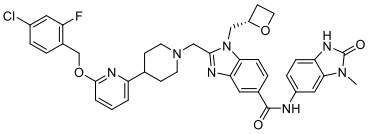
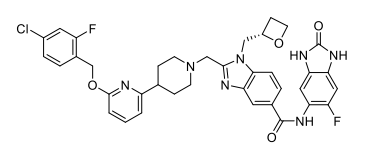


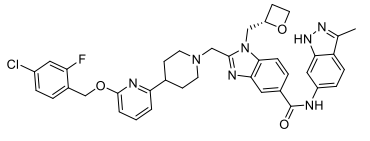
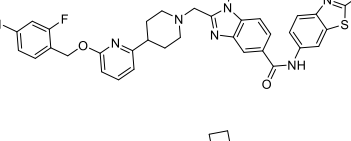
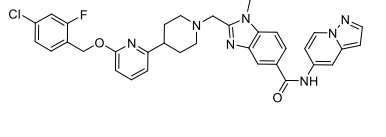
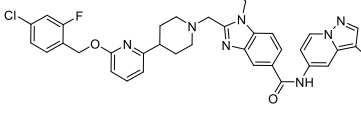
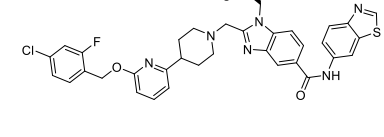
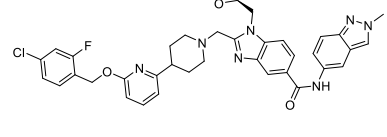
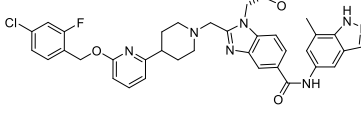
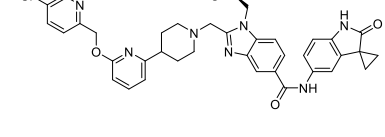
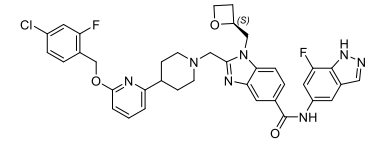
















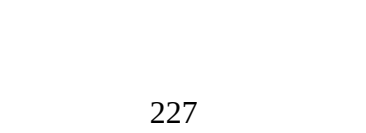










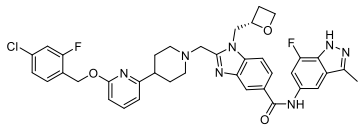
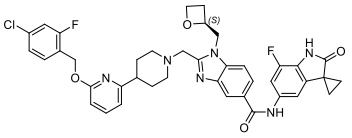
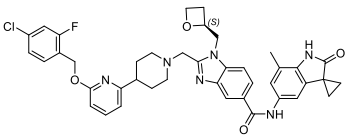
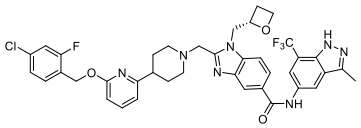
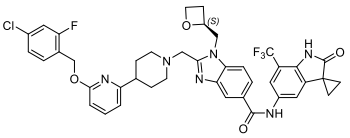
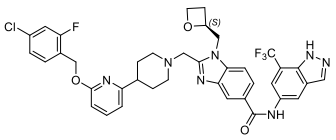
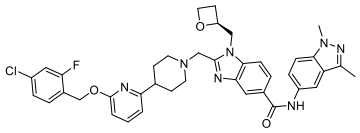
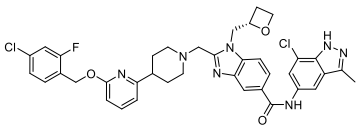
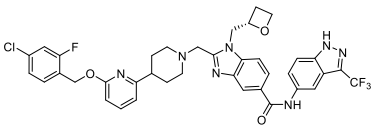
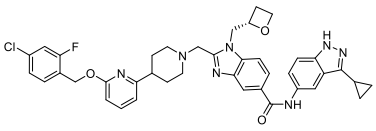
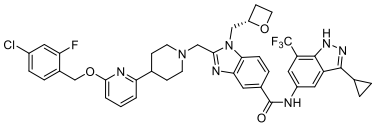
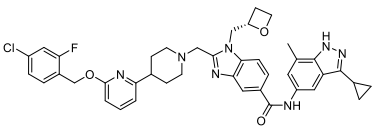
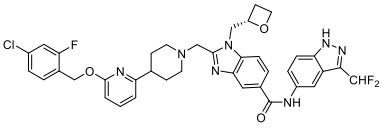
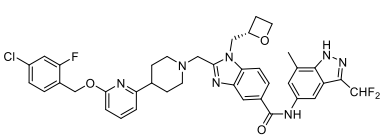
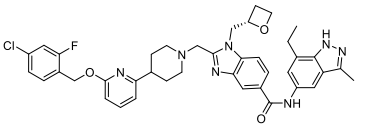
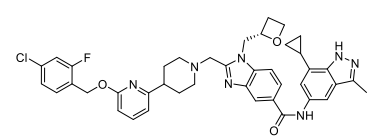
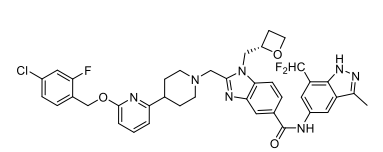
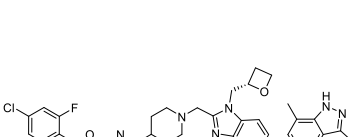
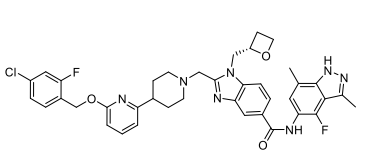
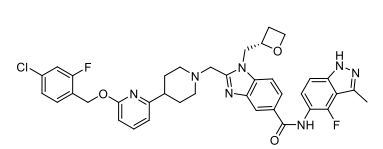
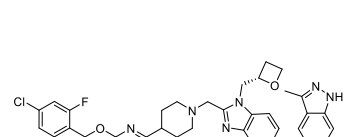
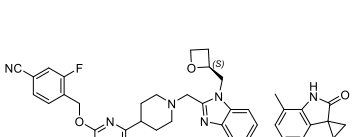
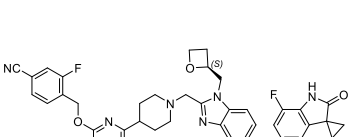
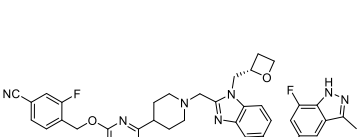




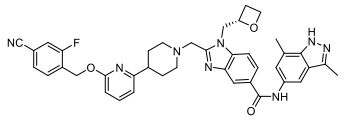
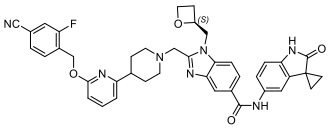
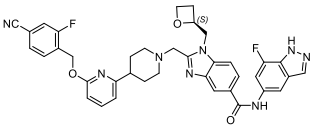
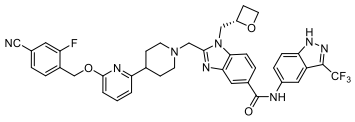
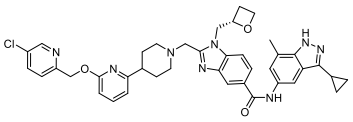
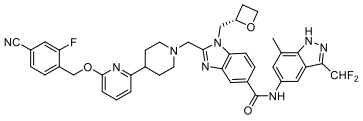
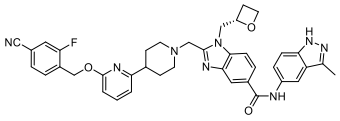
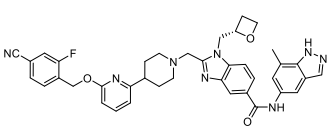
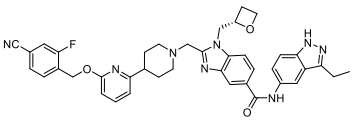
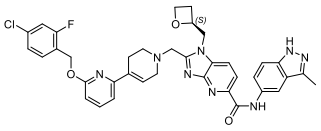
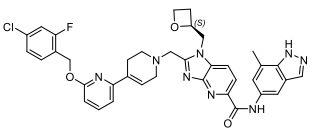
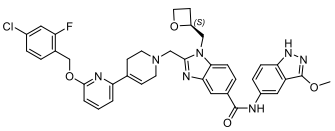
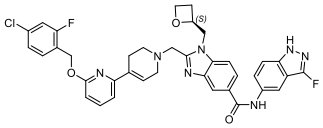
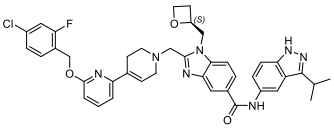
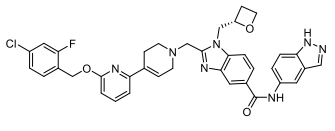
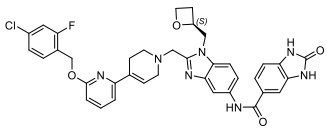
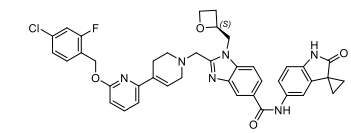
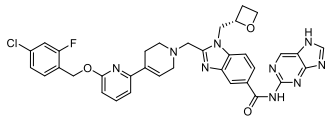
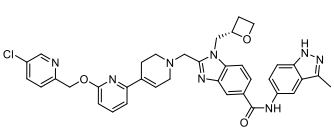
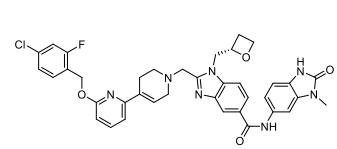
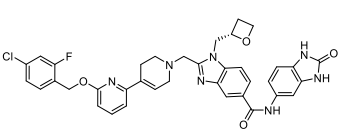
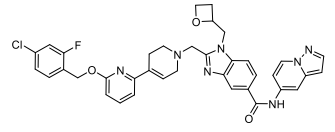
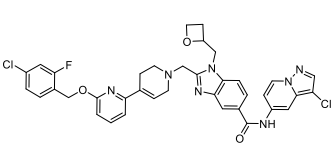
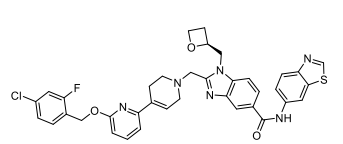
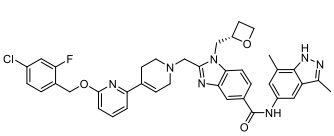
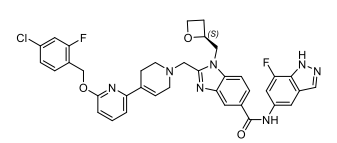
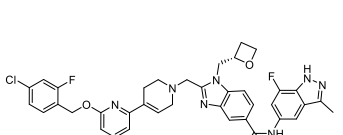
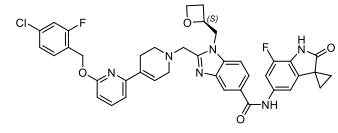
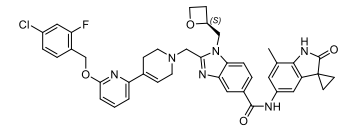
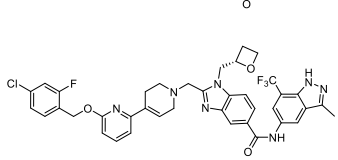
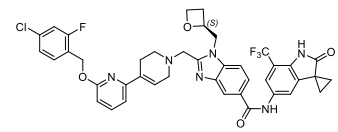
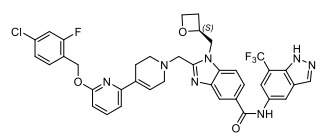
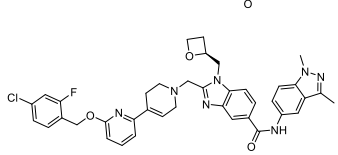















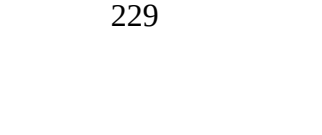










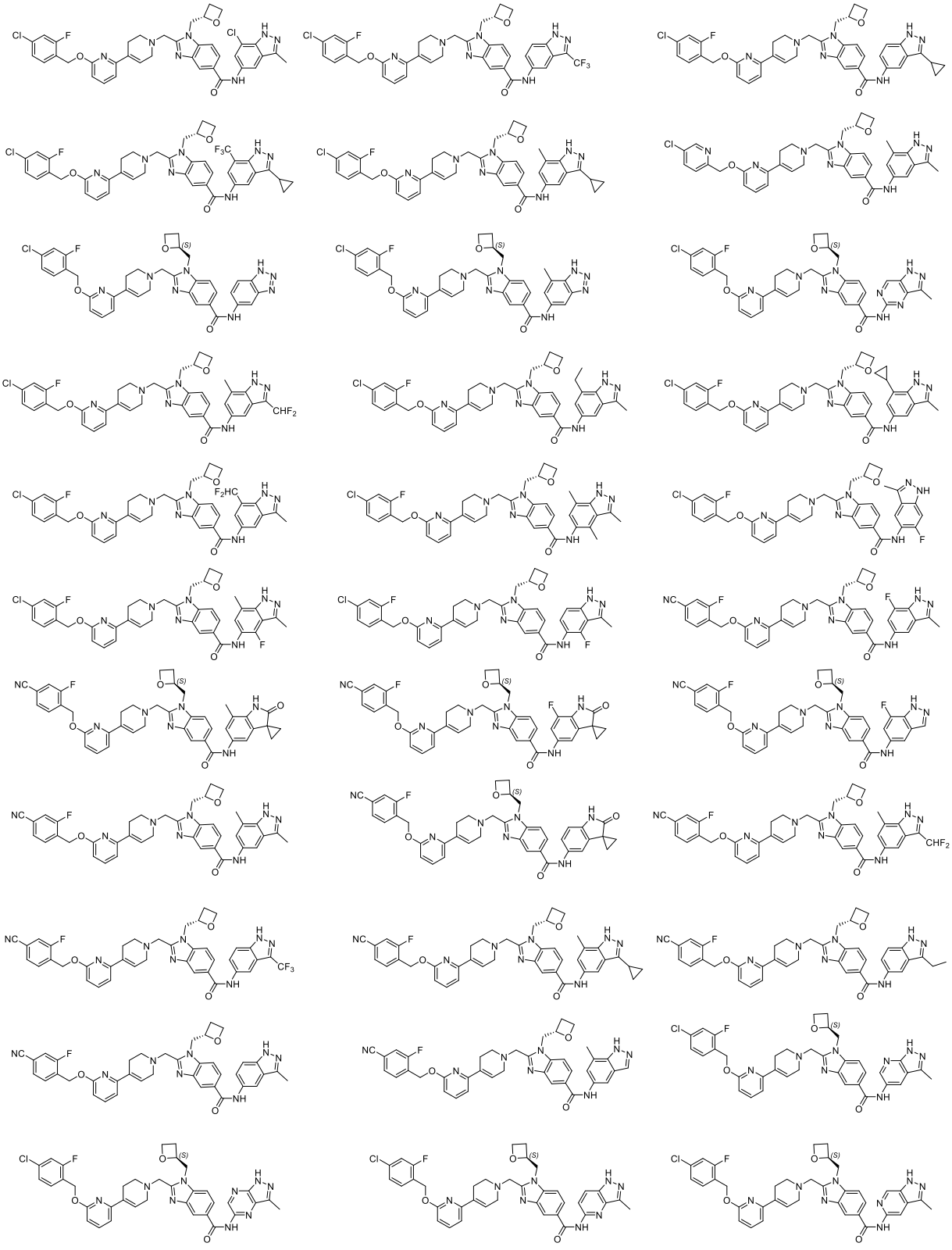


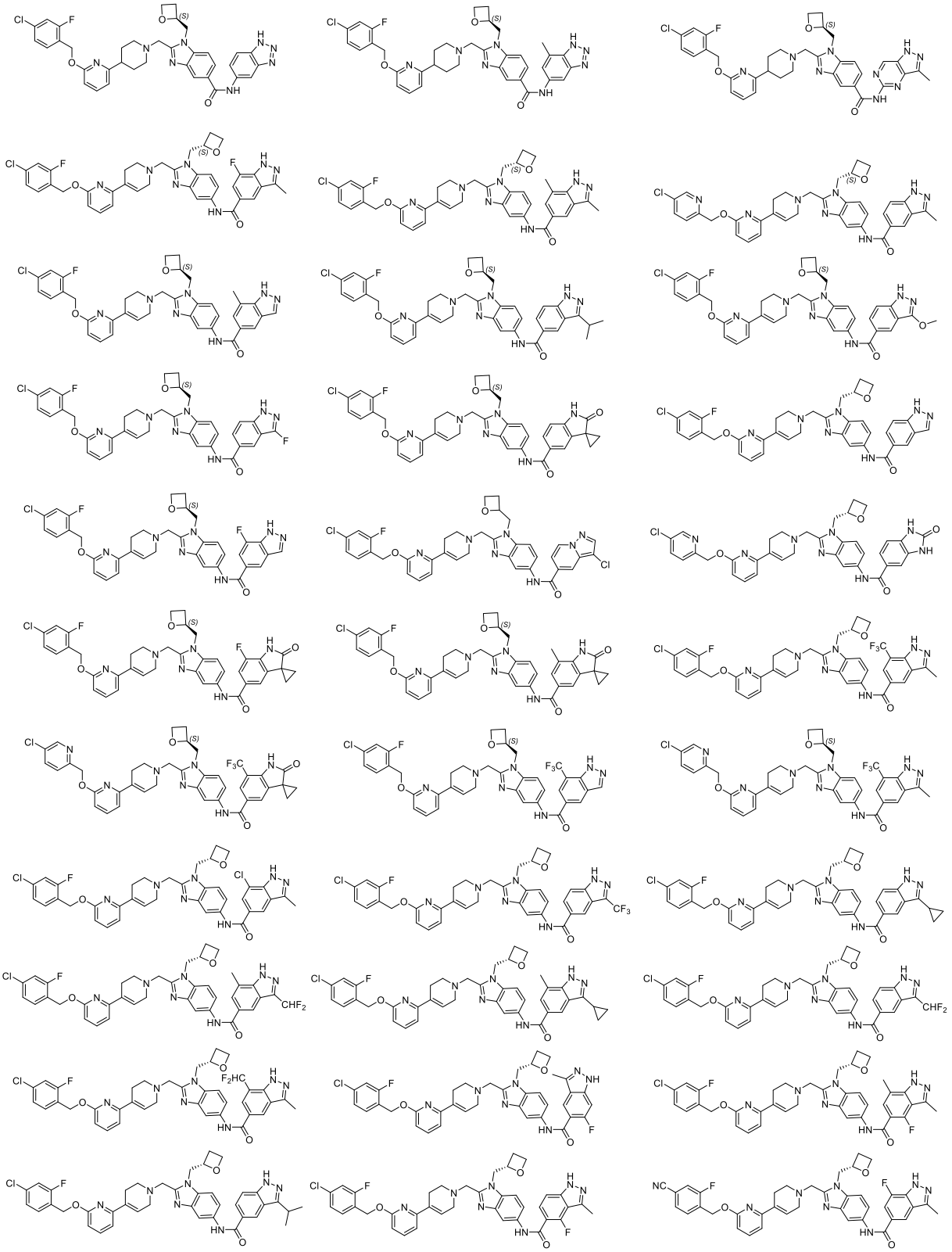

























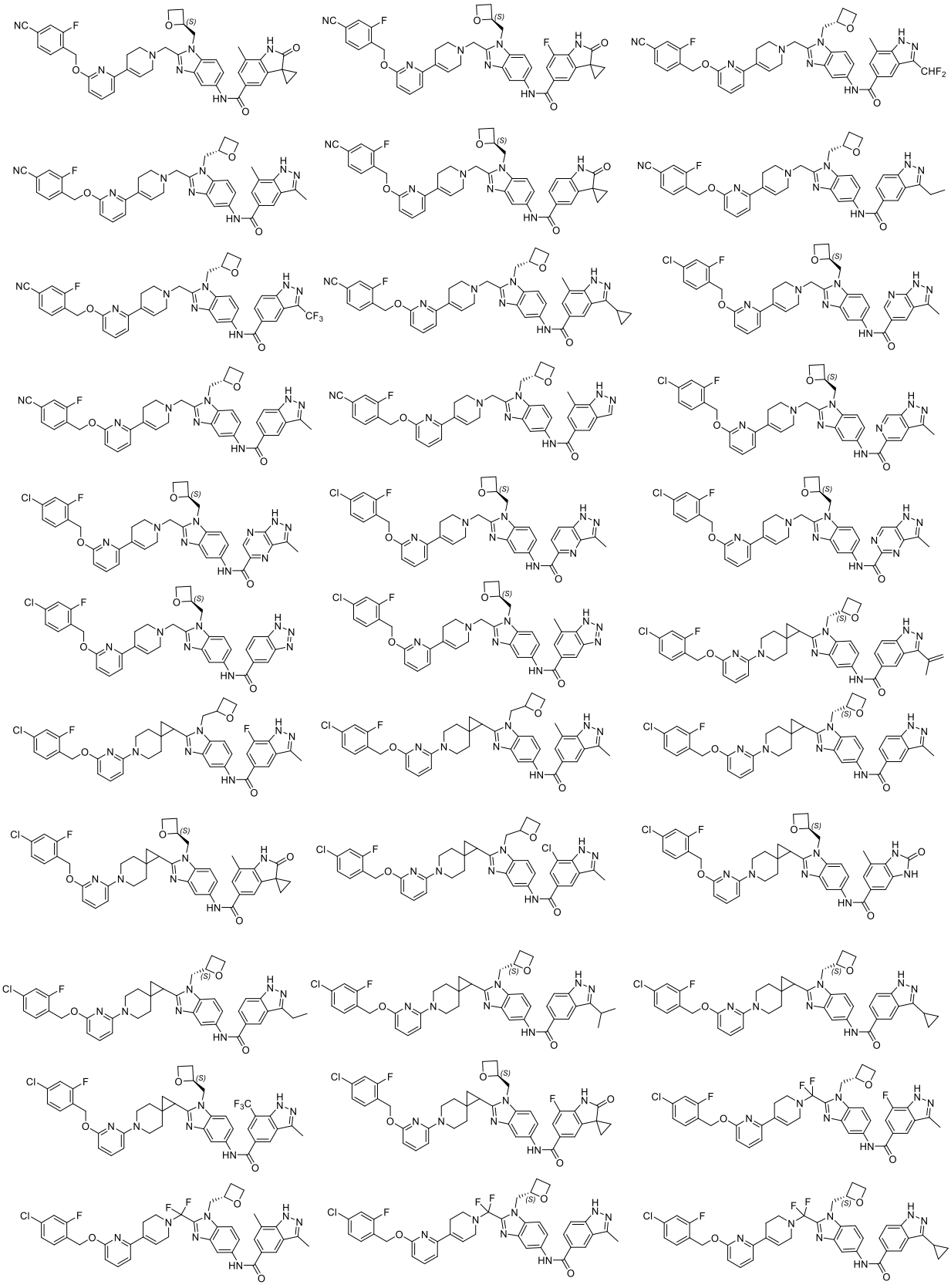


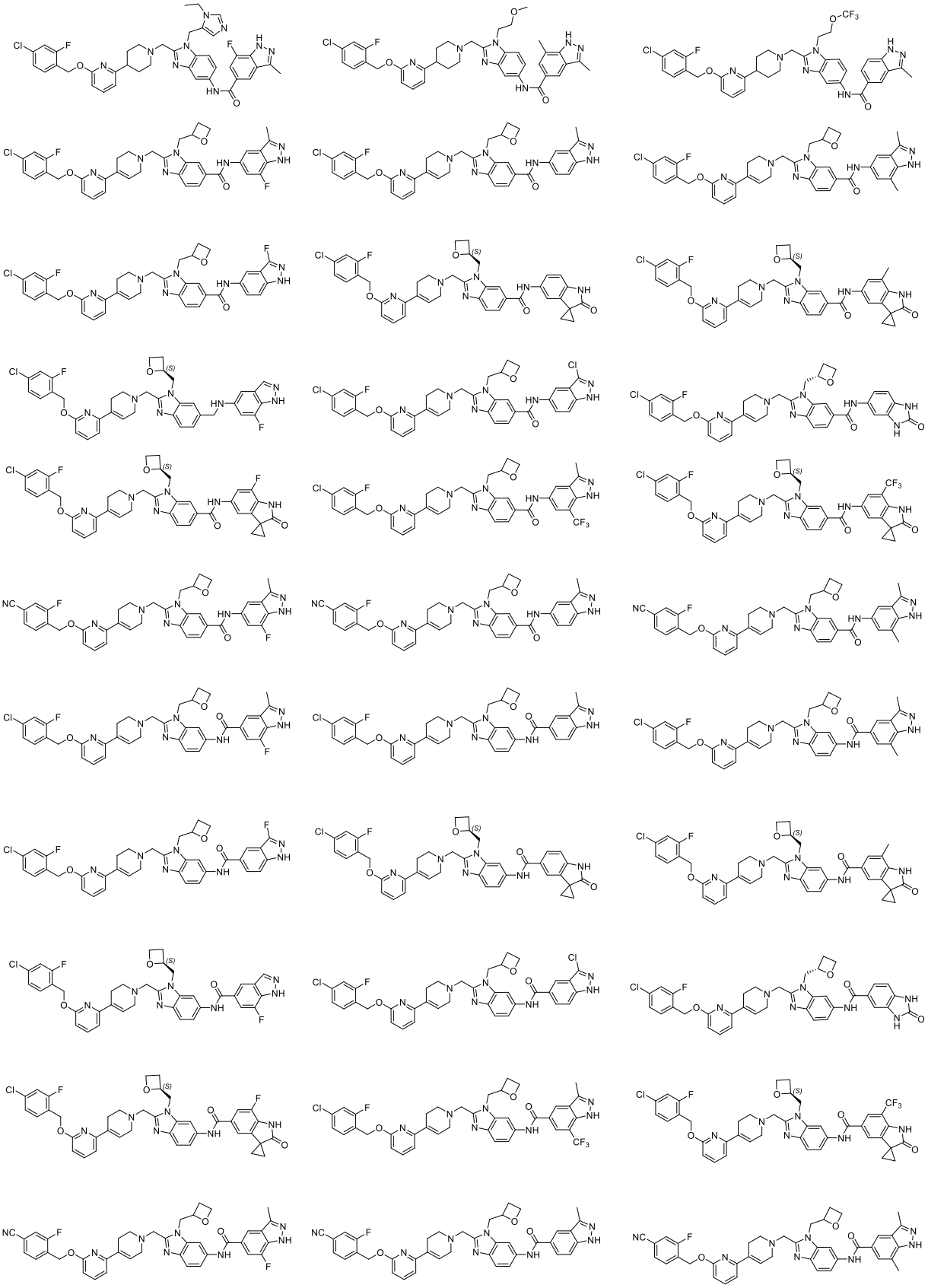


































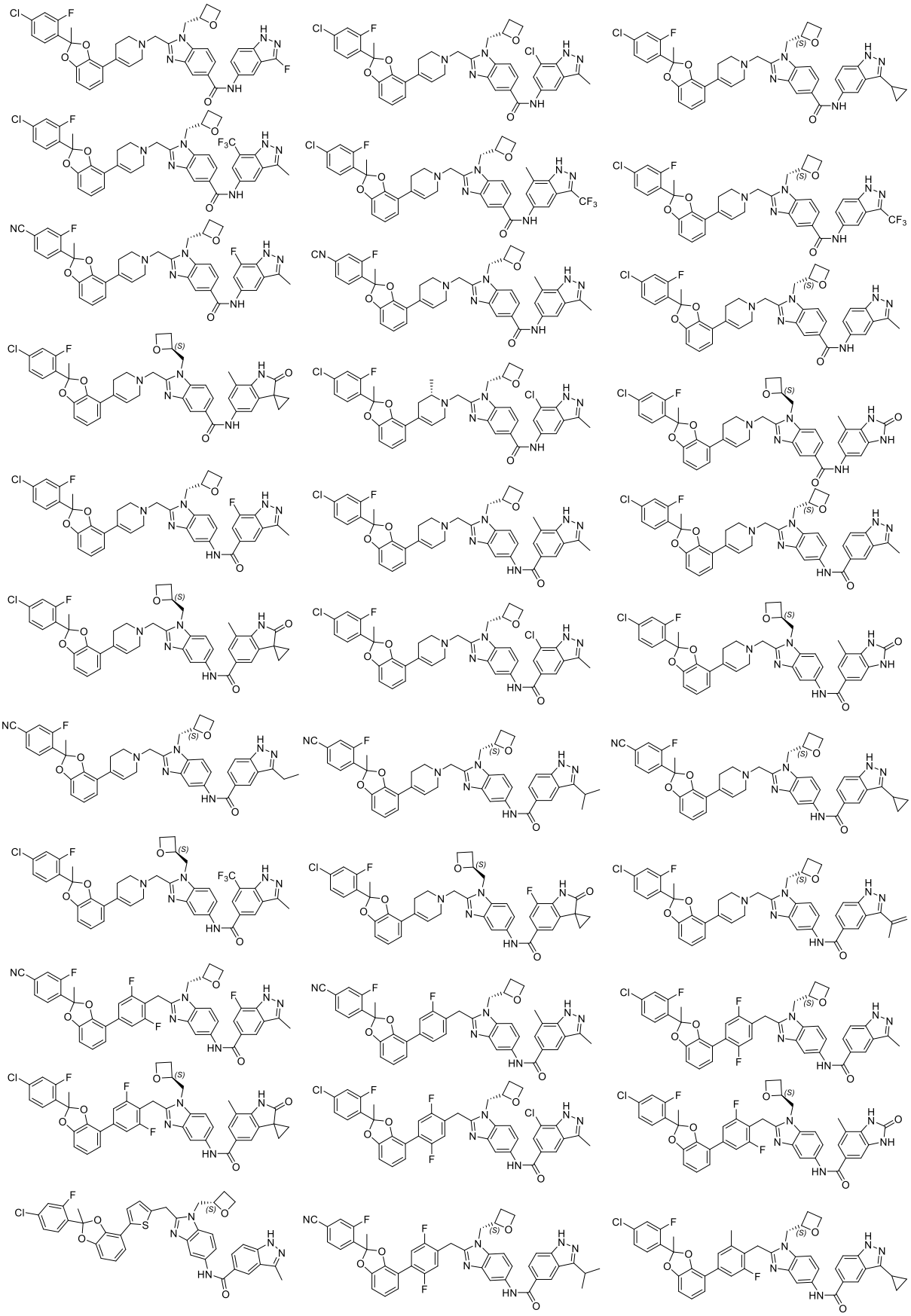


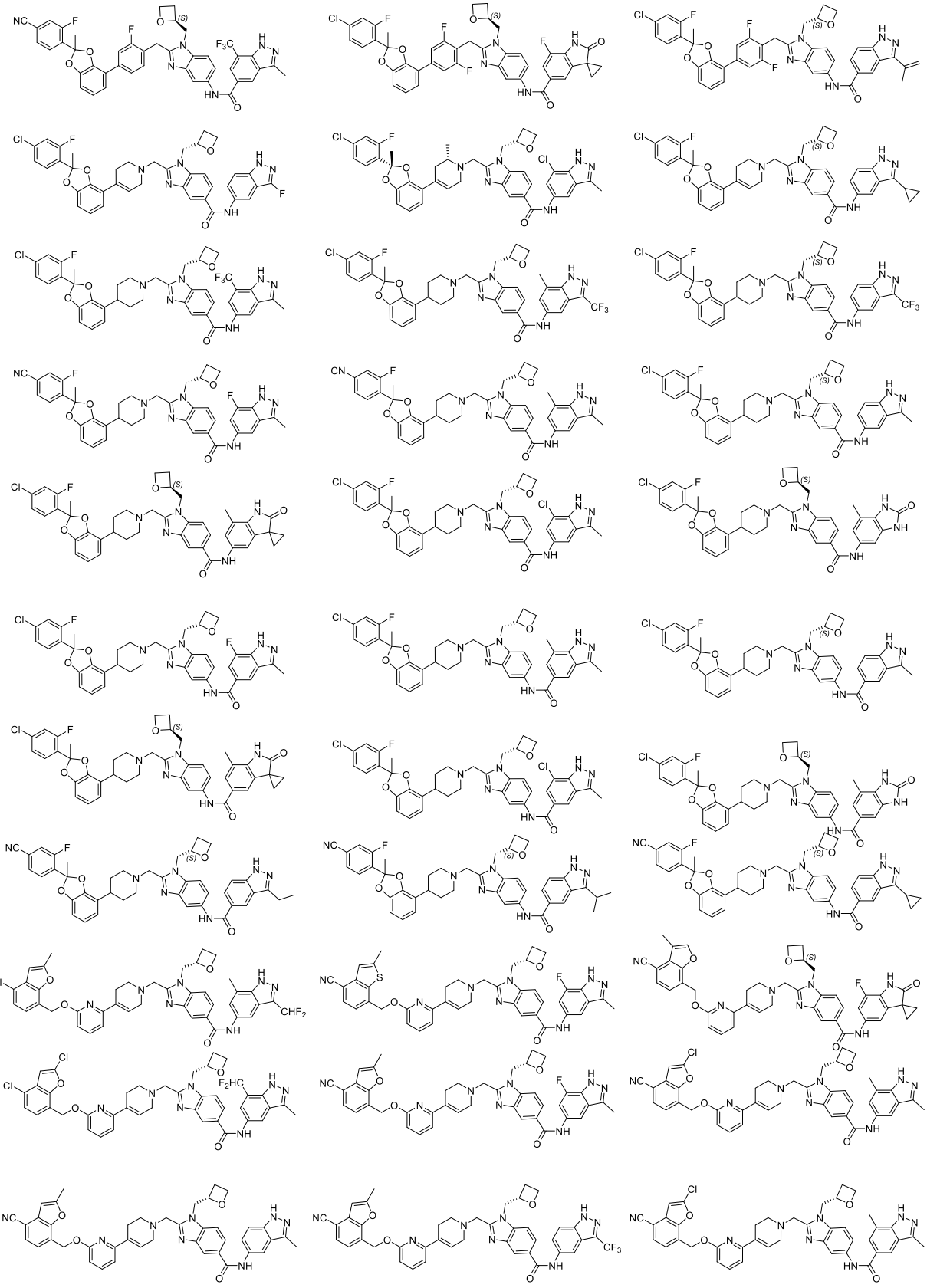


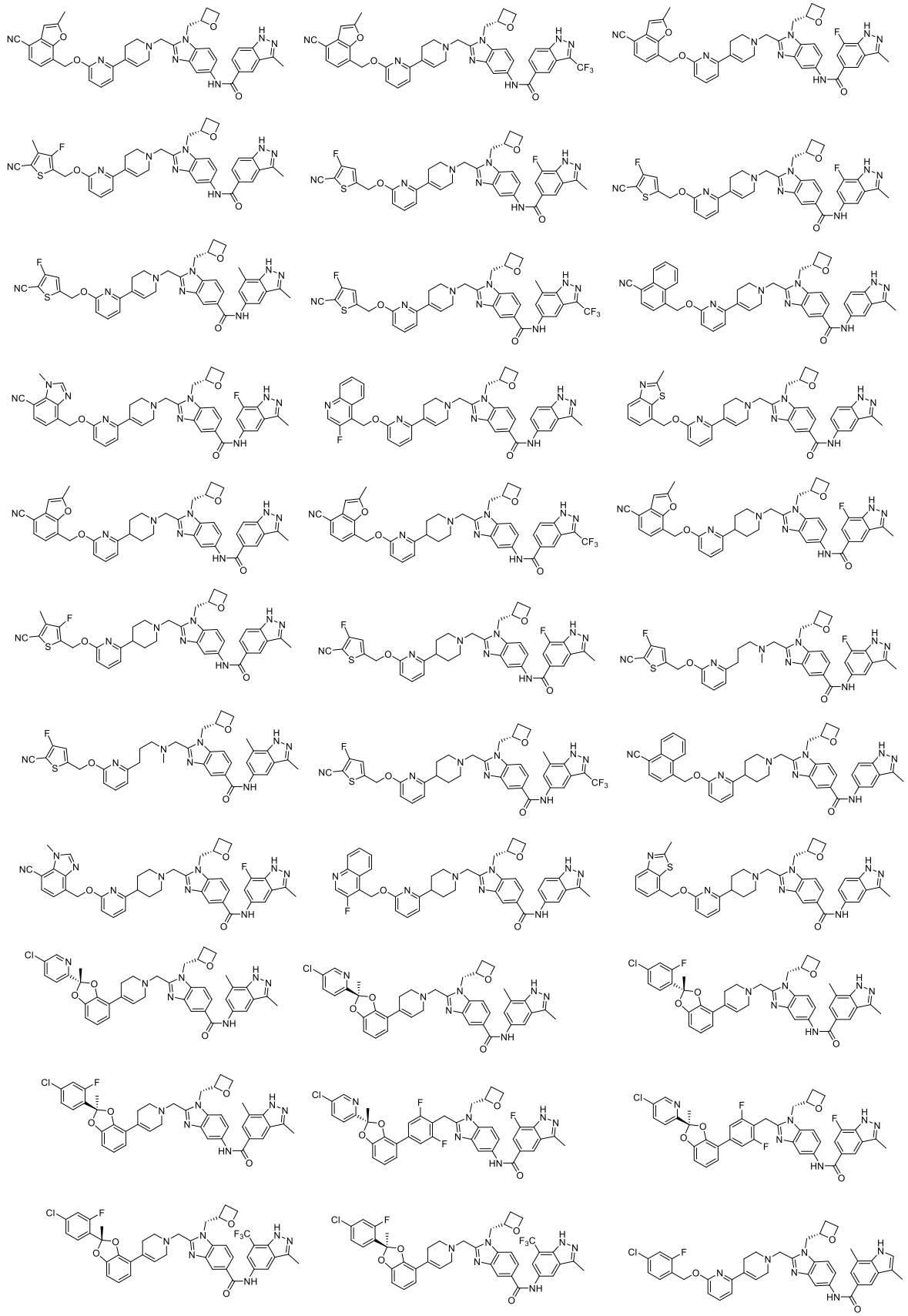


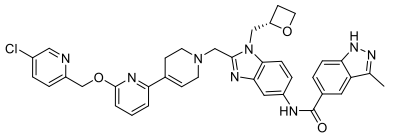
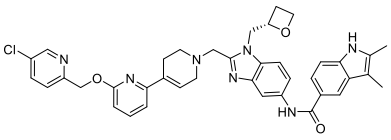
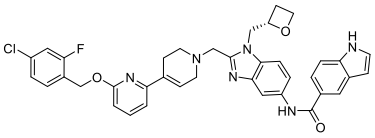
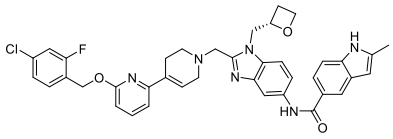
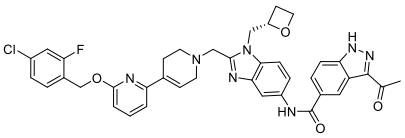
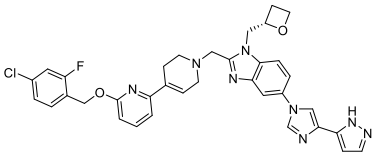
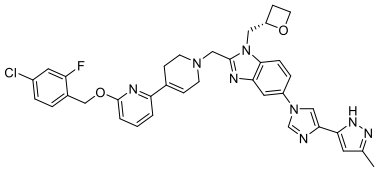
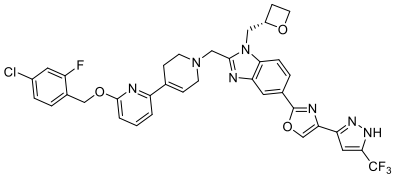
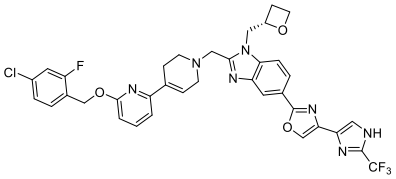
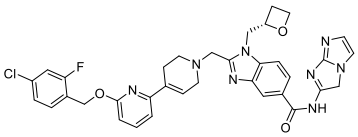
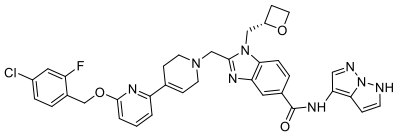
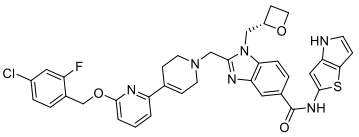
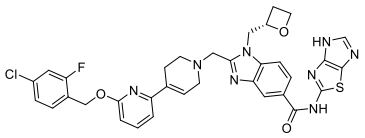
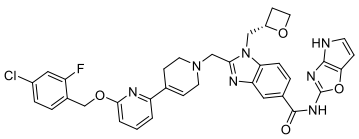
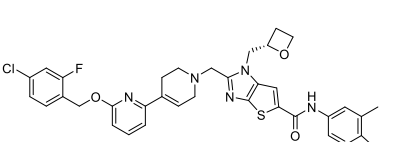
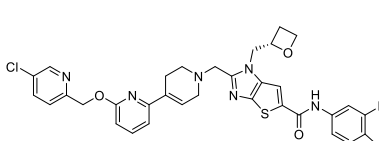
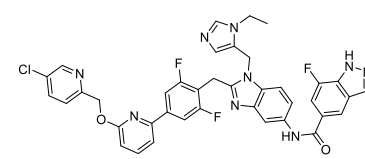
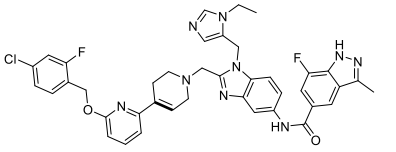
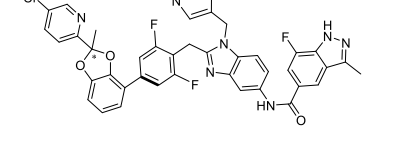
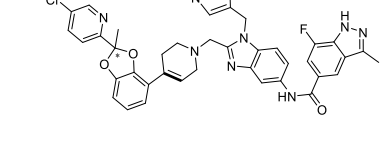
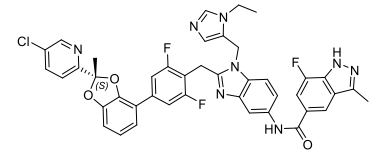
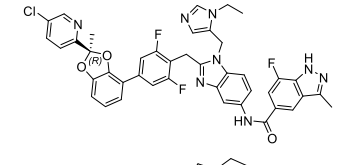
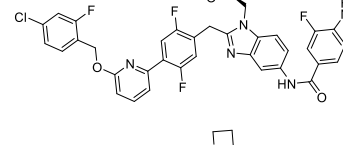
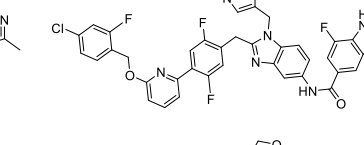
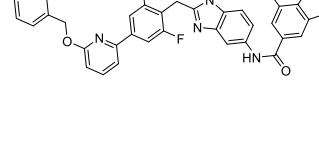
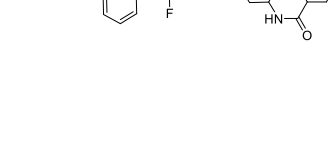











and

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9. A pharmaceutical composition, comprising the compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

10. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 9, for use in the treatment of a GLP-1R-mediated disease or condition, wherein the GLP-1R-mediated disease or condition is selected from the group consisting of T1D, T2DM, pre-diabetes, idiopathic T1D, LADA, EOD, YOAD, MODY, malnutrition-related diabetes, gestational diabetes, hyperglycemia, insulin resistance, hepatic insulin resistance, impaired glucose tolerance, diabetic neuropathy, diabetic nephropathy, kidney disease, diabetic retinopathy, adipocyte dysfunction, visceral adipose deposition, sleep apnea, obesity, eating disorders, weight gain from use of other agents, excessive sugar craving, dyslipidemia, hyperinsulinemia, NAFLD, NASH, fibrosis, cirrhosis, hepatocellular carcinoma, cardiovascular disease, atherosclerosis, coronary artery disease, peripheral vascular disease, hypertension, endothelial dysfunction, impaired vascular compliance, congestive heart failure, myocardial infarction, stroke, hemorrhagic stroke, ischemic stroke, traumatic brain injury, pulmonary hypertension, restenosis after angioplasty, intermittent claudication, post-prandial lipemia, metabolic acidosis, ketosis, arthritis, osteoporosis, Parkinson’s Disease, left ventricular hypertrophy, peripheral arterial disease, macular degeneration, cataract, glomerulosclerosis, chronic renal failure, metabolic syndrome, syndrome X, premenstrual syndrome, angina pectoris, thrombosis, atherosclerosis, transient ischemic attacks, vascular restenosis, impaired glucose metabolism, conditions of impaired fasting plasma glucose, hyperuricemia, gout, erectile dysfunction, skin and connective tissue disorders, psoriasis, foot ulcerations, ulcerative colitis, hyper apo B lipoproteinemia, Alzheimer’s disease, schizophrenia, impaired cognition, inflammatory bowel disease, short bowel syndrome, Crohn’s disease, colitis, irritable bowel syndrome, polycystic ovary syndrome and substance addiction.